

# MINIMALLY INVASIVE UROLOGIC SURGERY



EDITED BY  
ROBERT G MOORE · JAY T BISHOFF  
STEFAN LOENING · STEVEN G DOCIMO



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# Minimally Invasive Urologic Surgery

## Dedication

As in any endeavor many talented, dedicated people are involved and to single any one person out would misrepresent the total effort involved in this undertaking. Let it suffice that we thank Leonardo da Vinci, Galileo, and Albert Einstein, all of whom met with resistance in their undertakings but who persisted and succeeded because of their love and passion for their studies. Let us continue to make the reach greater than the grasp for the past, present, and future of this field we call endourology.

# **Minimally Invasive Urologic Surgery**

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## Preface

Acceptance of creative ideas, theories and even surgical techniques has often been met with skepticism and, at times, even outrage. This was certainly the case in the seventeenth century when Galileo asserted that the earth was round. The invention of minimally invasive urological techniques in the early 1990s was not received with enthusiasm by the urological community. Urologists appropriately demanded that these techniques prove themselves with surgical outcomes measured by the success of the procedure on the disease entity as well as associated morbidity, complication rates and effects on convalescences. All of the above variables were compared to the gold standard of “open” surgical procedures. Minimally invasive urologic techniques proved very quickly to have equal outcomes while significantly decreasing the postoperative morbidity and complication rate when compared to their open counterpart and over time have gained acceptance through reproducible and durable outcomes.

The purpose of this new surgical text is to share the experience gained by experts of urologic minimally invasive surgery in teaching techniques found to be effective and reproducible. It is our hope that this book will propagate the educational waves started by innovative, courageous surgeons who questioned long-standing, deeply rooted beliefs about surgical norms in order to decrease patient morbidity—before most urologists were ready to embrace those changes.

*Robert G Moore  
November 2004*



# **Part I**

The essentials of minimally  
invasive urologic surgery

# 1

## Endourology surgical anatomy\*

Brian K Auge and David M Albala

### Introduction

Endourology has come to the forefront of urologic surgery for the management of various stone and noncalculous conditions. With this, an increasing number of urologists are performing routine and complex endourologic procedures, all of which have the potential for significant patient morbidity. Understanding the anatomy and anatomic relationships of the urinary tract is, therefore, vital to minimizing complications and maximizing success rates. This chapter describes the basic anatomy of the male and female urinary systems and the relationships of urologic organs to surrounding structures. In addition, common congenital anomalies are discussed, with a focus on implications during endourologic procedures.

### Urethra

The urethra serves as a conduit for emptying of the urinary bladder and spans a distance from the bladder neck to the urethral meatus. Both male and female urethras are divided into sections with distinct landmarks. Due to the length of the urethra and the presence of the prostate gland, these landmarks are more prominent in men.

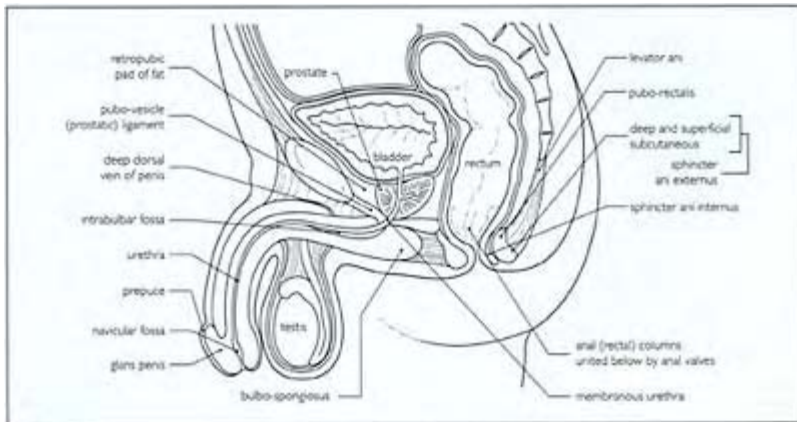
The male urethra can be divided into two distinct areas: the anterior and posterior portions. These areas are separated by the external striated sphincter or urogenital diaphragm (Figure 1.1), through which the membranous urethra traverses. The anterior urethra begins at the urethral meatus and is lined by squamous epithelium at its most distal extent, with transitional epithelium lining most of the remainder of the urethra. The fossa navicularis is a landmark within the glans penis, a point at which urethral strictures commonly occur. The penile, or pendulous, urethra is located within the shaft of the penis and contains the anteriorly located openings to the ducts of Littre (Figure 1.2). These ducts drain the small periurethral mucous glands. The bulbar urethra is a dilated portion of the anterior urethra, beginning approximately at the level of the suspensory ligament of the penis. The bulbar urethra lies within the bulb of the penis, surrounded by bulbocavernosus muscle, and ends at the distal portion of the external sphincter. The

\* The views expressed in this chapter are those of the authors and do not reflect the official policy of the United States Navy, Department of Defense, or U.S. Government.

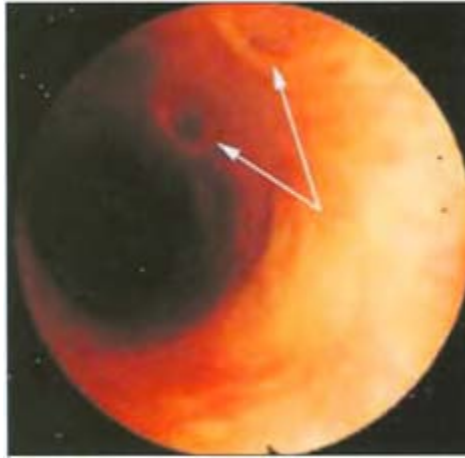
most common location for a traumatic urethral stricture is the bulbar urethra, as seen in the retrograde urethrogram shown in Figure 1.3.

The posterior urethra progresses from this location proximally to the bladder neck and is covered with transi-tional epithelium that is similar to that in the remainder of the collecting system. Frequently, during endoscopic procedures using local anesthesia, the sphincter may take on a diaphragm-like appearance. The prostatic urethra will vary in length and appearance depending on patient age and degree of benign prostatic hyperplasia. The verumontanum defines the apical aspect of the prostatic urethra (see Figure 1.3), with the ejaculatory ducts situated on the lateral surface of the verumontanum. As patients age, the lateral lobes of the prostate will encroach upon the urethral lumen, potentially contributing to bladder outlet obstruction. Occasionally, a median lobe or median bar will be encountered, distorting the location of the ureteral orifices and causing J-hooking of the distal ureter. This J-hooking can result in significant difficulty in catheterizing the ureteral orifice when retrograde procedures are performed, and can make visualization of the ureteral orifices difficult when transurethral resections of the prostate are performed.

The female urethra is located within the anterior vaginal wall and is significantly shorter than the male urethra, a characteristic possibly contributing to the higher incidence of stress urinary incontinence and infections in women. Inspection of the female urethra begins at the introitus. Placement of the endoscope into the urethra must be



**Figure 1.1** Sketch of the male pelvis, in median section. The external urinary sphincter separates the anterior urethra (distally) from the posterior urethra (proximally). The membranous urethra traverses the external sphincter.



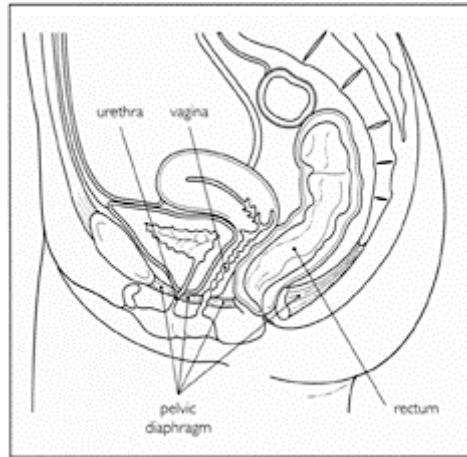
**Figure 1.2** Endoscopic view of the anterior urethra, depicting the ducts of Littre, indicated by the arrows.



**Figure 1.3** Retrograde urethrogram demonstrating a bulbar urethral stricture (arrow) secondary to a straddle injury to the perineum. Notice the narrowing of the striated sphincter proximal to the stricture, and the filling defect of the verumontanum.



accurate to avoid inadvertent vaginal endoscopy. The pink coapted appearance of the urethral mucosa and pale squamous appearance of the vagina enable the endoscopist to readily recognize proper positioning. The anterior and posterior components of the female urethra are distinct entities, yet less well defined. Again, these are separated by



**Figure 1.4** Anatomic relationships of the lower female urinary tract to surrounding structures.



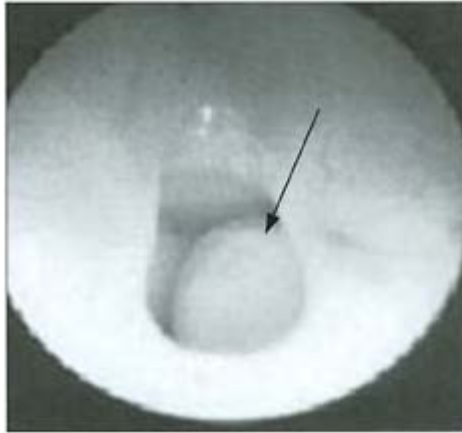
**Figure 1.5** Endoscopic view of the female urethra. Noted the coapted appearance of the highly folded appearance of the highly vascular mucosa.

the urogenital diaphragm as in the male counterpart (Figure 1.4). Coaptation of the folded urethra mucosa gives the female urethra a diaphragm-like appearance from the meatus to the bladder neck (Figure 1.5). Urethral diverticula develop, occasionally, most commonly in a posterior or posterolateral orientation. Calculi can occasionally be seen if the orifice is open to endoscopic inspection (Figure 1.6).

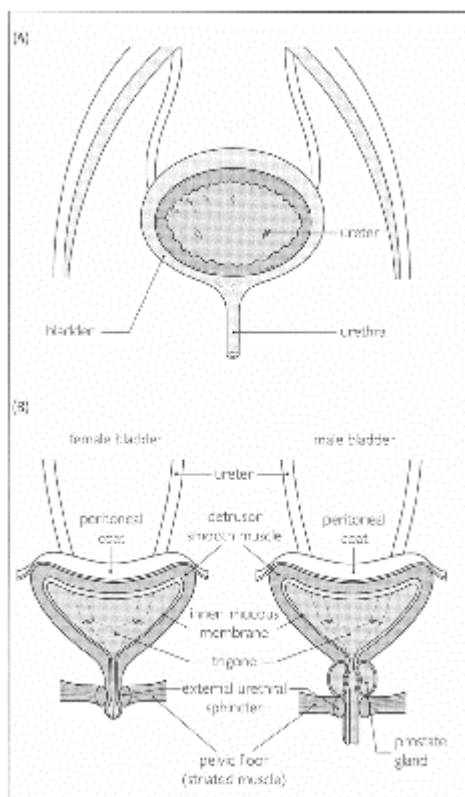
### Urinary bladder

The urinary bladder is a hollow organ with two basic functions: to store urine at low pressures and to empty urine completely on demand once capacity is reached. The bladder is composed of several smooth muscle layers: an outer serosal membrane and an inner 'mucosa', or lining of transitional epithelium. It is located extraperitoneally within the pelvis, with the uterus causing an extrinsic compression on the dome due to the cephalad position of the body of the uterus in relation to the bladder (see Figure 1.4). When fully distended, the bladder is palpable in most people. The bladder in an adult, when filled to capacity, holds approximately 350–500 ml of urine under normal conditions.

The ureteral orifices in their normal position are located on the floor of the bladder in a triangular area known as the trigone (Figures 1.7A and 1.7B), so named for its configuration with the ureteral orifices comprising the base of the triangle and the bladder neck serving as



**Figure 1.6** Urethral diverticulum with wide-open orifice and calculi (arrow) within the diverticulum. Urethral diverticula can cause symptoms of dysuria, dyspareunia and discharge or post-void dribbling, among others.



**Figure 1.7A** Schematic of the pelvic organs with the ureteral orifices, labeled ureter, located within the bladder on the trigone.

**Figure 1.7B** Comparison of the male and female urinary bladder.

the apex of the triangle. As the endoscope is passed into the bladder through the bladder neck, the scope must be directed laterally and posteriorly to identify the orifices. As mentioned previously, a large prostate can displace the ureteral orifices, especially when a large median lobe is encountered. Similarly, previous transurethral resection of the prostate or open pelvic surgery may have altered the anatomy. In a partially distended bladder, one can recognize the intertrigonal ridge connecting the two ureteral orifices.

The bladder is in close approximation to several important organs within the pelvis. The peritoneum and a portion of the intraperitoneal contents, namely the bowel, sit on the dome of the bladder. The uterus may slightly compress the cephalad portion of the bladder, which can be seen on plain film imaging. An obturator 'kick' can develop as a rapid and unexpected contraction of the adductor leg muscles when the obturator nerve is

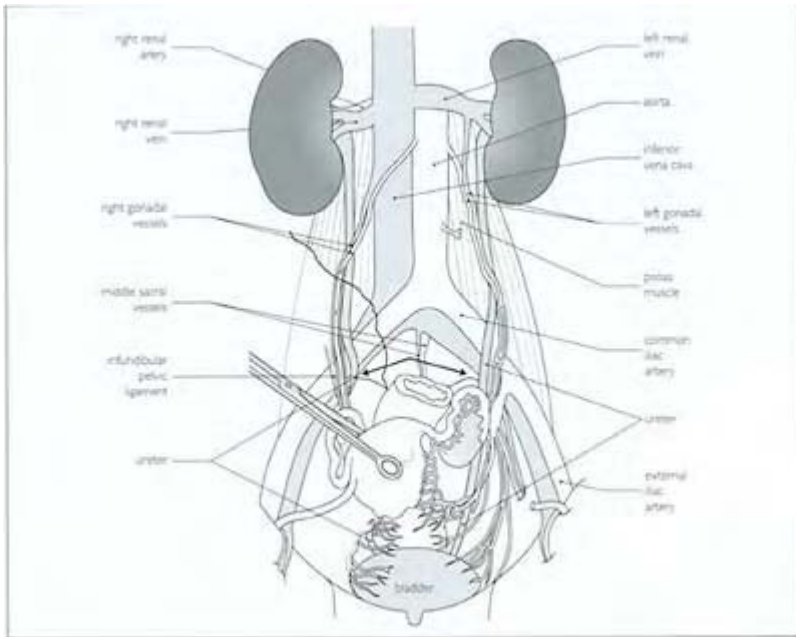
stimulated during resection of a lateral wall bladder tumor. The rectum is adjacent to the posterior bladder surface in a male, and the anterior vaginal wall is interposed between the bladder and rectum in the female pelvis.

## **Ureter**

The intrarenal collecting system is joined to the urinary bladder by the ureter, a completely retroperitoneal tubular structure (Figure 1.8). This is composed of both circular and longitudinal muscle fibers that enable the ureter to transport urine by peristalsis. The inner lining of transitional epithelium prevents absorption of fluid and electrolytes in the usual healthy state. Three natural points of narrowing exist: the ureteropelvic junction (UPJ), the ureterovesical junction (UVJ), and where the ureter crosses the common iliac vessels in the mid ureter. Urinary calculi will typically obstruct at one of these three locations if unable to pass spontaneously (Figure 1.9). Transitional cell carcinoma of the ureter can occur anywhere along the length of the ureter (Figure 1.10).

The ureter exits the renal pelvis at approximately the level of vertebral body L2. It proceeds vertically in the retroperitoneum along the lateral aspect of the transverse processes of the lower lumbar vertebrae to the sacrum. The ureter follows a path along the dorsal aspect of the retroperitoneum, crossing over the sacrum at the sacroiliac joint and into the true pelvis. Once in the pelvis, the ureter will course medially to enter the bladder just cephalad to the ischial spines. Figure 1.11 demonstrates these relationships as seen on intravenous urogram (A) and retrograde pyelogram (B).

Ureteropelvic junction obstruction (Figure 1.12), resulting in dilation of the renal pelvis and calyces with increased intrarenal pressures, can lead to renal insufficiency, calculus formation, recurrent infection, hematuria, and chronic pain. Causative factors include an aperistaltic segment of ureter, high insertion of the ureter on the renal pelvis, and crossing lower pole vessels, arteries, veins, or both (Figure 1.13). The location of the crossing vessels should be identified before an endopyelotomy is performed in order to avoid injury to these structures. Imaging modalities commonly utilized include computed tomography (CT) angiogram with three-dimensional reconstruction, endoluminal ultrasound (Figure 1.14), or, less commonly, plain angiography.



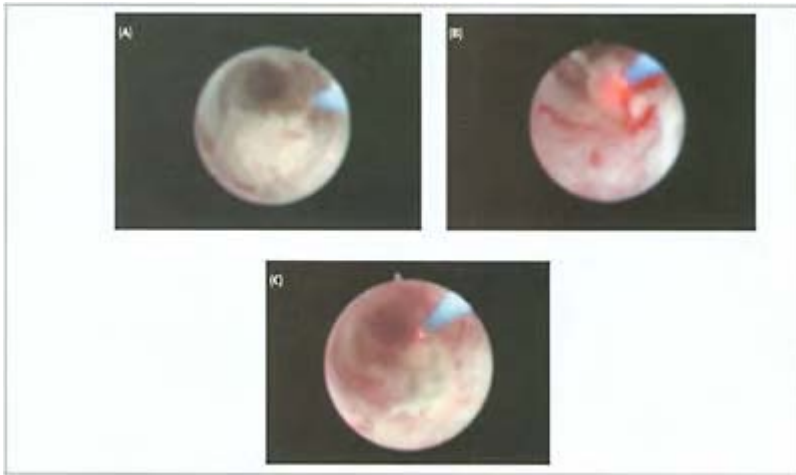
**Figure 1.8** Diagram of the retroperitoneal organs. Note the ureters as they cross over the common iliac arteries (arrows) and then dive deep into the pelvis to enter the bladder posteriorly at the trigone (not shown).



**Figure 1.9** Endoscopic view of a calculus within the ureter being broken with the laser.

### Intrarenal collecting system

The kidneys are situated within the retroperitoneum encompassed by Gerota's fascia. They are oriented so that the lateral aspect of the kidney is rotated posteriorly. The intrarenal collecting system consists of the renal pelvis and calyces, lined with transitional epithelium. The normal urine volume for a calyx ranges from 2.5 to 5 ml (Figure 1.15). The renal pelvis is the structure most posterior to the renal hilum, with the renal artery situated between the vein (anterior) and pelvis. The 10–15 calyces divided between upper pole, lower pole, and mid-polar regions are oriented in an anterior and posterior direction. This is important for obtaining percutaneous access, which typically is reached through a posterior route to avoid intra-abdominal



**Figure 1.10** Intraluminal transitional cell carcinoma of the ureter amenable to holmium laser ablation: tumor prior to (A), during (B), and after (C) laser ablation.

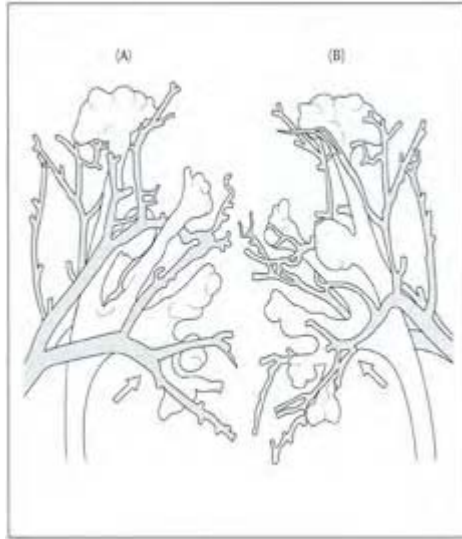


**Figure 1.11** Intravenous urogram (A) and retrograde pyelogram (B) delineating the normal radiographic appearance and pathway of the ureter from the renal pelvis to the bladder.



**Figure 1.12** Left ureteropelvic junction obstruction. The ureter is of normal caliber and the intrarenal

collecting system is markedly dilated proximal to the stricture.



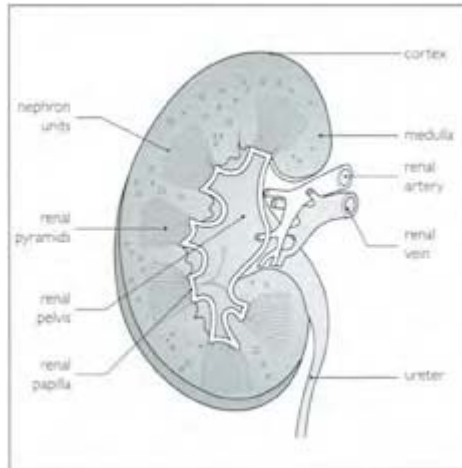
**Figure 1.13** Casts of the intrarenal collecting system and vasculature demonstrating lower pole crossing vessels both ventrally (A) and dorsally (B).



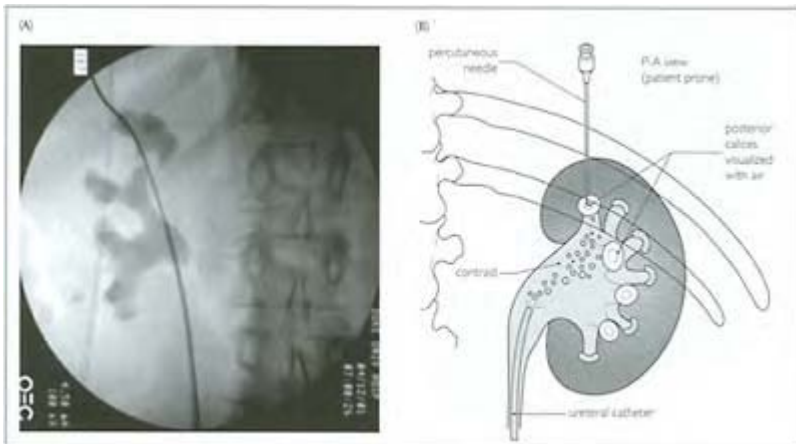
**Figure 1.14** Endoluminal ultrasound revealing crossing vessels at the ureteropelvic junction. Large arrow



indicates ureteral lumen and dashed arrow localizes the crossing vessel.



**Figure 1.15** Schematic of intrarenal collecting system and vasculature of the renal hilum. The renal vein is the most anterior structure, followed by the renal artery and renal pelvis.



**Figure 1.16** Percutaneous access is obtained through a posterior calyx with the patient in the prone position.



**Figure 1.17** Plastic model of the renal collecting system demonstrating the ability of the flexible ureterscope to access calculi within the lower pole.



**Figure 1.18** Access into a calyceal diverticulum can prove to be difficult in manipulating a wire through the stenotic infundibulum to achieve transureteral access.

contents (Figure 1.16). In both the upper and lower pole of the kidney are complex calyces, whereas the mid portion of the kidney has only simple calyces.

With the advent of the actively deflectable flexible ureteroscopes, complete inspection of the intrarenal collecting system can be performed routinely without much difficulty. Pathology not previously accessible not only can be visualized but also can be managed

with lasers, baskets, or graspers (Figure 1.17). Stenosis of the infundibulum draining a calyx can lead to diverticulum formation and subsequent calculus formation, intermittent pain, hematuria, or infection (Figure 1.18). Difficulty can be experienced in attempting to access this stenotic infundibulum either from an antegrade or retrograde approach.

### **Summary**

A complete and clear understanding of the anatomic relationships of the parts of the urinary tract is necessary for performance of efficient and effective endourologic procedures. Knowledge of the various permutations, from both a radiologic and endoscopic point of view, is invaluable in allowing the urologist to perform these procedures safely.

## 2

# Urologic laparoscopic anatomy

Jaime Landman and John G Pattaras

### Introduction

The breadth of urologic pathology that can be managed via the laparoscopic approach continues to expand as technologies and surgical experience mature. Mounting evidence has demonstrated that for many urologic procedures pathology can be managed efficiently and effectively while significantly decreasing the pain and convalescence traditionally associated with ablative and reconstructive open urologic procedures.

The blossoming of laparoscopic surgery within urology has resulted in some challenges as the most common procedure, laparoscopic nephrectomy, remains technically demanding. Unlike our general surgery colleagues who commonly perform simple ablative procedures such as cholecystectomy, the urologic surgeon must traverse the learning curve of laparoscopic surgery on a steep and slippery slope.

One of the challenges of learning laparoscopic surgery remains the novel perspective on well-known anatomy. For thousands of years clinical anatomists (surgeons) have admired and described anatomy from the 'outside in.' Using direct vision, palpation, and an external perspective, the human body has been precisely characterized. Similarly, traditional medical education has focused on the teaching and learning of anatomy in this manner. Laparoscopic surgery, however, presents a novel perspective on a traditional science.

The laparoscopic surgeon must work in a twodimensional world with limited haptic feedback. While initially counter-intuitive, limiting, and perhaps frustrating, the technology associated with laparoscopic surgery permits the experienced laparoscopic surgeon a view that may be considered superior to that of the traditional surgical approach. While generally still providing two dimensions, currently available laparoscopes provide excellent optics and lighting. The standard laparoscope provides the surgeon a well-lit surgical field and a magnification 12 times better than use of the naked eye. Having once mastered this technology, the surgeon experiences a wealth of exquisite anatomic detail that cannot be appreciated without technological enhancement. Superior visualization of structures allows some compensation for limited tactile feedback. The laparoscopic surgeon relies on detail such as alteration in the weave of suture material to determine tension during laparoscopic suturing.

While not intended to be an inclusive and complete anatomic description of urologic anatomy, this chapter will focus on assisting the experienced urologic surgeon to transition to the 'inside out' view of laparoscopy.

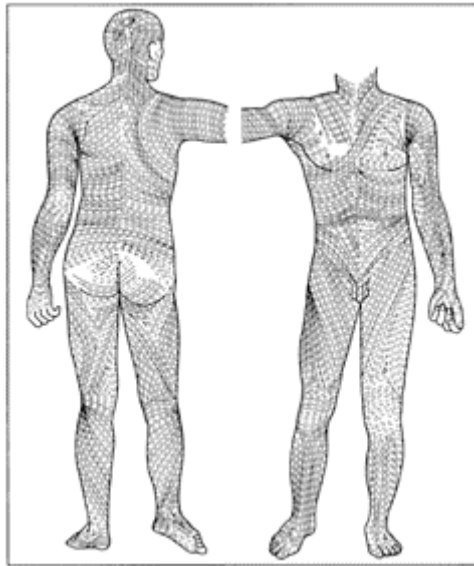
## Body surface anatomy

Successful laparoscopic surgery is based on trocar access. Like open surgery, the thoughtful choice of location and type of incision is crucial to surgical outcome. However, unlike traditional open incisions, trocar sites cannot be extended to provide superior exposure, and additional retraction cannot be placed to improve access.

Thoughtful trocar placement incorporates parameters that include the surgical objectives, anatomic considerations, and body habitus. While trocar placement templates are available for each procedure, trocar positioning must be individualized for each patient, the location of the pathology, and surgeon preference. Laparoscopic surgical experience will refine the ability of each surgeon to establish optimal access.

### *Skin incision*

At the present time, all trocar access requires a skin incision. Trocar incisions should be made along natural skin cleavage lines (Langer's). These lines define the prevailing arrangement of connective tissue fibers and are evident as crease lines in the skin (Figure 2.1). Incisions created along lines of Langer yield superior cosmetic results. The vast majority of urologic pathology is accessed via the torso



**Figure 2.1** Langer's lines are natural skin cleavage lines.

where the lines of Langer run circumferentially around the torso. Thus, incisions should be made in a transverse direction to optimize healing.

The umbilicus is a common site for laparoscopic access. Trocar placement may be above or below the umbilicus, depending on the surgical target, and access should be made via a curvilinear incision. The incision itself should be as close to the umbilicus as possible, as healing will usually result in contraction that will yield an almost undetectable scar.

### *Surface anatomy*

Key surface landmarks for urologic laparoscopic access are the umbilicus, the anterior superior iliac spine, the costal margin, and the 12th rib. These important surface landmarks help the urologic surgeon to choose appropriate trocar access sites and orient the surgeon to the underlying visceral anatomy. Another important structure, the rectus abdominus muscle, may be difficult to appreciate by inspection or palpation. Consequently, the laparoscopic surgeon is obliged to estimate the location of the rectus margin. Moreover, abdominal access through the rectus abdominus muscle is a relative contraindication because the epigastric vessels run through the muscle, and potentially may be injured.

### **Umbilicus**

The umbilicus is an optimal site for laparoscopic access. Because the umbilicus is centrally located, it will usually provide an intuitive perspective for laparoscopic visual orientation. Cosmetically, it is a superior site, as a curvilinear incision made close to the umbilicus will frequently retract into the umbilicus. When the patient is in the supine position, the umbilicus is an excellent site for primary access to the peritoneal cavity because the peritoneum is closest to the skin at this point on the abdominal wall. The properitoneal layer of fatty tissue, which lies between the linea alba and the peritoneum, is thinnest at the level of the umbilicus. Moreover, the umbilicus is an excellent extraction site for intact removal of renal tumors.

In establishing umbilical access, special consideration should be given to the patient with an extremely obese or very thin body habitus. When Hurd and colleagues evaluated the relationship of the umbilicus to the aortic bifurcation using magnetic resonance imaging (MRI) and computed tomography (CT),<sup>1,2</sup> they assessed the effect obesity has on this relationship. In non-obese patients weighing less than 160 lb (73 kg), the umbilicus is a mean distance of 0.4 cm caudal to the aortic bifurcation, with a skin-to-peritoneum distance of 2 cm. In obese patients weighing between 160 and 200 lb (73 and 91 kg), the umbilicus is 2.4 cm caudal to the aortic bifurcation, with a skin-to-peritoneum distance of 2 cm. In obese patients weighing more than 200 lb (91 kg), the umbilicus is located 2.9 cm caudal to the bifurcation of the aorta, with a skin-to-peritoneum median distance of 12 cm. The authors concluded that Veress needle insertion in the non-obese patient should be at a 45° angle from the horizontal in order to reduce the risk of major abdominal vascular injury and properitoneal placement. Because of the increased distance to the peritoneum in the obese patient, and the caudal displacement of the umbilicus in relation to the aortic bifurcation, the Veress needle should be inserted at a 90° angle from horizontal to achieve intraperitoneal placement. In the overweight patient, an angle

between 45° and 90° from horizontal will allow satisfactory intraperitoneal placement of the Veress needle.

### **Anterior superior iliac spine**

The anterior superior iliac spine is an excellent surface landmark as it is easily discernible even in the most obese patient. Many urologic procedures are performed with the patient in the lateral decubitus position. Trocar placement at a site just cephalad and medial to the anterior superior iliac spine is useful because this is a common left-handed working site for laparoscopic procedures. The anterior superior iliac spine is a site of attachment for the internal oblique, external oblique, and transversalis fascial layers. Penetration of the abdominal wall is facilitated at this site by the 'tenting-up' of the abdomen by this bony prominence.

### **Costal margin**

When the patient is in the lateral decubitus position, a similar 'tenting' effect is noted at the costal margin. Thus, another common primary trocar placement site is in the anterior axillary line below the costal margin. In the lateral decubitus position, this site is useful as a right-handed working trocar site. Primary access to the peritoneal cavity at this site is similarly facilitated by the 'tenting' effect of the attachment of the abdominal wall fascial layers to the costal margin. As the inferior edge of the liver may extend below the costal margin, care should be taken at this site to prevent liver laceration.

### **Twelfth rib**

Retroperitoneal access in the flank position is usually gained through an incision just caudal to the tip of the 12th rib. The 12th rib is usually discernible by palpation. In the very obese patient, the surgeon may estimate the location of the 12th rib. Digital palpation and dissection of superficial fatty layers through a small incision will allow localization of the 12th rib in the majority of patients and will facilitate properly positioned primary renal access.

### **Body habitus/obesity**

There are multiple physiologic and anatomic alterations that occur with obesity. Fat distribution will frequently alter the choice of access sites. Abdominal fat may be distributed primarily in the form of a pannus, or the patient may have a more even 'barrel-like' distribution of fat. The operating surgeon should assess fat distribution after the patient is properly positioned.

When the patient is in the lateral decubitus position, a large pannus may frequently fall medially, allowing the surgeon to enter laterally through a relatively thin abdominal wall. In these cases the umbilicus may fall far to the contralateral side and should not be utilized as an access site. Medial access may be obtained at any site lateral to the margin of the rectus abdominus muscle; the location of this margin must frequently be estimated.

In contrast, the more evenly distributed 'barrel-like' body habitus may have little change in the position of the umbilicus relative to the midline.

Another anatomic consideration in the obese patient is the ability to tolerate pneumoperitoneum. For many pelvic procedures laparoscopic access to deep pelvic structures (i.e. bladder, pelvic lymph nodes, or prostate) may be achieved only with a steep Trendelenburg position. In the obese patient the steep Trendelenburg position may result in an excessive weight of abdominal contents on the diaphragm, which may result in increased inspiratory pressures and hypercapnea. Decreasing insufflation pressures and reducing the steep Trendelenburg position may allow laparoscopic procedures to progress in some cases.

### **Previous surgery/scars and adhesions**

Abdominal scars from earlier surgery or trauma should be noted by the laparoscopic surgeon. Access sites for earlier laparoscopic procedures occasionally may be difficult to discern because small (<5 mm) trocar sites frequently result in subtle scar formation. Although laparoscopic access should be achieved with great care in all patients who have undergone abdominal surgery, previous laparoscopic procedures will have resulted in significantly less scar formation,<sup>3</sup> and surgical access in patients who have undergone prior laparoscopic surgery is usually uncomplicated.

In patients who have undergone open surgery, laparoscopic access is usually easy to obtain at a site distant from the surgical scar. Special attention should be given, however, to patients having undergone complicated procedures associated with infectious processes, significant inflammation, peritonitis, or urinoma formation. These patients will more frequently have significant diffuse and dense adhesions, which may make any access challenging and hazardous. The effect of previous abdominal surgery on perioperative outcomes in patients undergoing a renal/adrenal laparoscopic procedure via a transperitoneal approach was recently reviewed. The authors found that a previous open abdominal operation increased the risk of laparoscopic operative and major complications, which mostly resulted in increased length of hospital stay.<sup>4</sup> The ipsilateral location of the open prior surgical scar impacted the laparoscopic access complication rate.

Often, adhesions resulting from earlier procedures may be avoided by altering the surgical approach. After abdominal surgery, access to the kidney, ureter, and pelvic structures can frequently be obtained using an extraperitoneal approach. Similarly, patients who have had extraperitoneal surgery (i.e. percutaneous nephrolithotomy) can be approached transabdominally to avoid areas of heavy scarring.<sup>5,6</sup> Prior open abdominal or renal surgery had once been considered a relative contraindication to laparoscopic surgery in the past. Because of the likelihood of adhesion formation and perinephric scarring, there is a greater difficulty of obtaining access to the peritoneal cavity and surgical dissection. Chen et al.<sup>6</sup> retrospectively looked at 24 patients who had prior significant open or renal surgery. They were able to complete all secondary laparoscopic cases successfully and concluded that, with experience, laparoscopic urologic surgery can be performed in a safe timely manner.

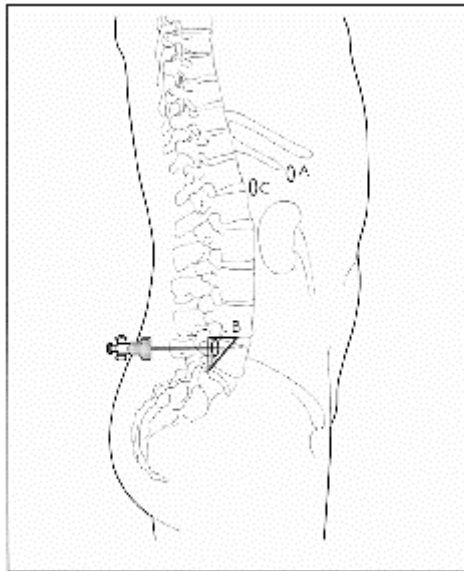


## The retroperitoneum

Most urologic pathology is of extraperitoneal origin. Because adrenals, kidneys, ureters, prostate, and urinary bladder are all extraperitoneal structures, the anatomy of the retroperitoneum is particularly important to the urologic surgeon.

Laparoscopic transperitoneal anatomy is intuitive and comfortable for the urologic surgeon as the space is filled with easily identifiable fixed organs and structures, which can continuously orient the surgeon. In contrast, the retroperitoneum is characterized by fatty tissue, which initially is disorienting to the surgeon because anatomic landmarks are not always immediately visible. However, with the experience of a few cases, the retroperitoneal approach becomes more comfortable.

The retroperitoneal approach to the kidneys and upper urinary tract has been popularized by several endourologists.<sup>7-9</sup> Initial access is gained via a 1.5–2.0 cm incision created at the tip of the 12th rib, inferior or superior lumbar triangle (Figure 2.2). After blunt penetration of the

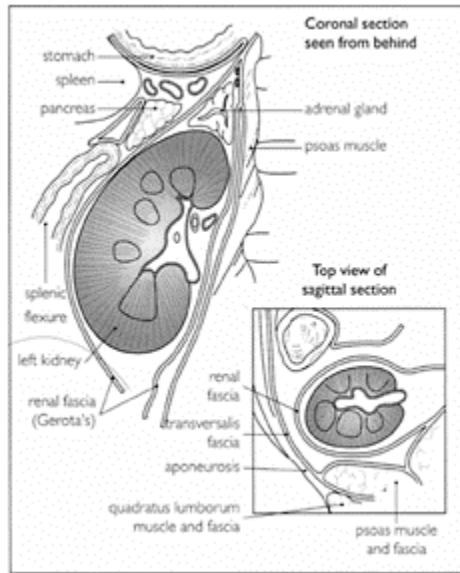


**Figure 2.2** Initial access sites for retroperitoneoscopy: tip of 12th rib (A), inferior (B) or superior lumbar triangle.

lumbodorsal fascia, the retroperitoneal space is initially created by digital palpation. Using digital palpation at this site, the surgeon can identify the psoas muscle posteriorly and the lower aspect of Gerota's fascia (Figure 2.3). The psoas muscle is the most important landmark in the retroperitoneum. This muscle may be used for orientation both by digital palpation and laparoscopic vision.

The psoas muscle originates from the lateral aspects and transverse processes of the vertebral bodies and discs (T12 to L4) and has a characteristic appearance. Distally, the psoas muscle fuses with the iliac muscle to form the ileopsoas muscle. The longitudinal striations and tendon of the psoas muscle are easily visible through the fascia that invests this muscle. After developing the retroperitoneal space via blunt and/or balloon dissection, the ureter and gonadal vessels are evident as they transverse the 'lower cone' of Gerota's fascia. These structures are useful for orientation landmarks of the retroperitoneum.

Retroperitoneal fat has a characteristic appearance and typically will be easy to dissect bluntly with minimal bleeding. However, patients with a history of surgery or inflammatory responses in the retroperitoneum may have fibrosis of the retroperitoneal fat that may make blunt dissection challenging. Using the access site at the tip of the 12th rib, the surgeon can usually identify the peritoneum and bluntly mobilize it medially to provide additional



**Figure 2.3** Both transverse and coronal sections of Gerota's fascia and the kidney delineates its relationship to adjacent organs and structures.

working space in the retroperitoneum for secondary trocar placement. Immediately after access, the renal hilar pulsations are frequently visible by slight cephalad orientation of the laparoscope. On the left side, the lumbar vein is the most posterior and the first vessel of the renal hilum to be visualized. Gentle dissection of the fat in this region will disclose the renal artery. From this viewpoint the renal vein usually can be found immediately behind the renal artery. Occasionally, the location of the renal vasculature is difficult to

discern. In these cases the lower pole of the kidney within Gerota's fascia can be identified. The dissection can then proceed cephalad along the psoas muscle to identify the renal hilum, much like the transperitoneal approach to the renal hilum.

A major advantage to the retroperitoneal approach is the avoidance of complicated adhesions from prior transperitoneal surgery. One can approach the peritoneum from an initial retroperitoneal access (see Figure 2.2). This is a safe approach in which the peritoneum is carefully examined and entered at a point where it is thinnest. This allows lysis of adhesions and direct visual placement of intraperitoneal trocars. This form of access should be considered the approach of choice for the patient with a history of abdominal surgery undergoing laparoscopic renal surgery.<sup>5</sup>

Renal anatomy is familiar territory to all urologists. However, the magnification and excellent illumination afforded by the laparoscopic approach reveal a fine level of detail that is not appreciable with traditional open surgery. The anatomic relationships of the kidney with surrounding structures are easily appreciated via the transperitoneal approach (see Figure 2.3).

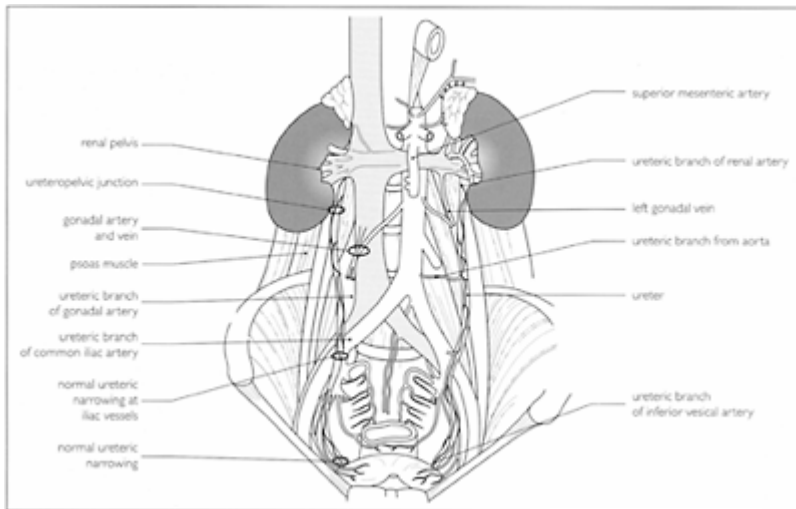
### **Right kidney**

In the flank position, gravity mobilization of the small intestine occurs and allows for visualization of the kidney within Gerota's fascia as a bulge under the ascending colon. Classically, the attachment of the colon to the abdominal wall has been inaccurately referred to as the 'Line of Toldt.' In fact, laparoscopic inspection reveals clearly that the ascending colon is attached to the abdominal sidewall via a thin mesentery. This mesentery is not a 'line,' but rather is a band that can range in width from several millimeters to several centimeters. Typically, the band is 1–2 cm in width and can be best appreciated by gently sliding a laparoscopic instrument lateral to the colon. The 'band of Toldt' is typically separate from the anterior surface of Gerota's fascia, and the two layers can be seen sliding over each other. Also, the band can be identified by characteristic linear capillaries that run from the abdominal sidewall to the lateral edge of the colon (see Figure 2.4). Initial careful dissection will allow the surgeon to enter the avascular plane between the colon and Gerota's fascia. Usually, this plane is most distinct, and thus technically easiest to establish, at the lower pole of the kidney.

Once the plane has been established, the colon and the colonic mesentery can be mobilized medially to expose the anterior surface of Gerota's fascia. The mesenteric fat has a distinct color and character. The mesenteric fat can be identified laparoscopically as much more distinctly yellow than Gerota's fascia. The mesentery is also more friable and has a tendency to bleed with manipulation. Even minor bleeding noted during the dissection of the plane between the colonic mesentery and Gerota's fascia should alert the surgeon that his plane of dissection is too medial. Superiorly, separation of the colon from Gerota's fascia can be challenging to dissect as the inferior edge of the liver commonly is draped over this area. Mobilization of the liver's edge and superior retraction of the liver are very helpful in identifying and dissecting upper pole structures. For adequate mobilization of the liver, incision of the triangular ligament connecting the lateral margin of the liver to the diaphragm is necessary. Incision of the triangular ligament should be performed with care to avoid diaphragmatic injury.

As the colonic mesentery is mobilized, the medial portion of the anterior Gerota's fascia becomes evident. As the dissection proceeds medially and posteriorly, the duodenum should become evident. Occasionally, it will appear that the vena cava has been identified. However, the duodenum will always be anterior to the vena cava. The surgeon should actively seek the duodenum after medial mobilization of the colon has been initiated. Usually the duodenum is quite obvious as a pink to purple bowel structure. Occasionally, the duodenum can be decompressed and confused with Gerota's fascia. Careful inspection to identify the duodenum will help avoid injury. The Kocher maneuver can be performed to gain access to the vena cava and renal vein. Using cold sharp dissection with scissors or the harmonic scalpel, which has minimal peripheral energy spread, is suggested to initiate duodenal mobilization, as there is little space between the duodenum and Gerota's fascia. After sharp incision of most lateral attachments of the duodenum to Gerota's fascia, there typically is only loose areolar tissue connecting these structures. Therefore, the surgeon can gently apply a blunt sweeping medial motion to complete the Kocher maneuver after the initial sharp mobilization. Attempting to bluntly push the duodenum off of Gerota's fascia without starting this dissection sharply may lead to duodenal injury.

Adequate mobilization of the duodenum and colon results in exposure of the lateral margin of the vena cava (Figure 2.5). Inferiorly, the gonadal vein is usually readily identified, inserting on the lateral aspect of the vena cava below the renal hilum. The gonadal vein may be sacrificed if necessary, but preservation of the gonadal vein should be attempted even with radical renal surgery. Transection of

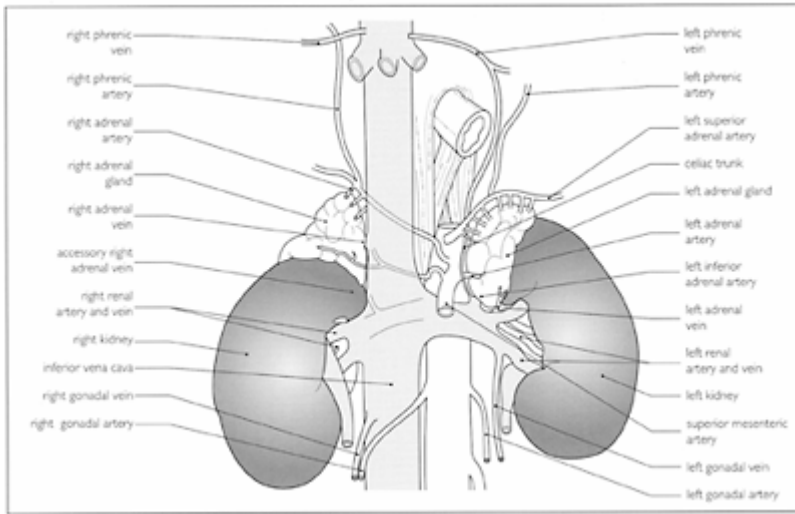


**Figure 2.4** Anatomic relationship between kidney, ureter, psoas muscle and great vessels. Three areas of ureteral narrowing are demonstrated.

the gonadal vein in the male will occasionally result in testicular pain. While this pain is transient, sparing the gonadal vein is optimal. If significant bleeding is encountered during medial mobilization of the lower pole, it is likely that the surgeon has transected or avulsed the gonadal vein off of the vena cava. As the insertion of the gonadal vein into the vena cava is quite delicate, it has been referred to as 'the angle of sorrows.' Further lateral dissection of the lower pole of the kidney will reveal the inferior tail of Gerota's fascia, which rests on the psoas major muscle. Laparoscopically, the psoas major muscle is a useful anatomic landmark. Inspection of the psoas major muscle will reveal characteristic muscle bundles, the psoas tendon, and the genitofemoral nerve. Following the psoas major muscle will help delineate the lower pole of the kidney within Gerota's fascia. At the level of the lower pole of the kidney, the ureter can be identified lateral to the gonadal vein on the surface of the psoas muscle (Figure 2.4). The ureter is another structure that it is useful to identify before dissection of the renal hilum, as anterior and lateral traction on the ureter will help identify the location of the hilum. Although laparoscopic surgery results in oliguria, the ureter maintains its characteristic peristalsis, which is useful to distinguish the ureter from the gonadal vein.

After mobilization of the colon and duodenum, and dissection of the lower pole of the kidney, the lateral edge of the vena cava usually is easily identified. In thin patients with little retroperitoneal fat, the medial aspect of the vena cava, contralateral renal vein, and aorta are frequently discernible. Identification of the gonadal vein and ureter can be helpful in orienting the laparoscopic surgeon. Renal vein abnormalities such as duplication are uncommon, but are much more common on the right side. The right renal vein is usually located at the level of the inferior edge of the liver. Consequently, releasing the cephalad traction on the liver and inspecting its lower edge will provide a useful clue as to the location of the renal vein. Lumbar branches of the right renal vein are uncommon, and the right adrenal vein typically drains directly into the vena cava. Keeping these 'anatomic textbook' descriptions in mind, the laparoscopic surgeon should dissect the right renal vein with great care, as laparoscopic vascular control can be challenging.

The renal artery is located posterior to the renal vein (see Figure 2.5). The availability of high-quality imaging with CT and MRI scans is very helpful in preoperatively delineating the renal hilar anatomy. The renal artery is commonly posterior to the renal vein, but it may be directly behind, slightly cephalad, or slightly caudal to the renal vein. Imaging can also help identify early medial



**Figure 2.5** Blood supply of kidney and adrenal gland derived from the aorta and inferior vena cava.

branching of the main trunk of the renal artery. Complete dissection of the renal vein is occasionally helpful to identify the location of an elusive renal artery. Superior to the renal hilum the adrenal gland is positioned between the kidney and vena cava within a sheath of Gerota's fascia. Adrenal anatomy is described in the Adrenal glands section of this chapter. Posteriorly, the right Gerota's fascia is attached to the psoas and quadratus lumborum muscles by flimsy tissues.

Within Gerota's fascia the kidney is located under a variable layer of perinephric fat. Of interest, the amount of perinephric fat surrounding the kidney does not always correlate with the exterior appearance of the patient (see Figure 2.3). Careful inspection of CT or MRI scans can help the surgeon determine the amount of perinephric fat that will be present. In patients with a large amount of perinephric fat, a nephrectomy specimen for a small kidney may be quite large, and even very exophytic masses may be difficult to discern laparoscopically. Thus, the amount of perinephric fat has significant clinical impact on the level of difficulty associated with laparoscopic renal procedures. The perinephric fat is easily separable from the capsule of the kidney, and the renal capsule is usually separable from the renal parenchyma with minimal bleeding. In patients with a history of surgery, tumors with desmoplastic reactions, infections, or inflammatory processes, these planes may be quite adherent and difficult to separate.

### Left kidney

When the patient is in the lateral decubitus position, gravity mobilization of the small bowel results in exposure of the left kidney within Gerota's fascia as a mass under the

descending colon. The 'line of Toldt' is identified as previously described. However, there is a physiologic adhesion in the left upper quadrant that anchors the left kidney to the abdominal wall. This adhesion is present in the majority of patients without a history of surgery or an abdominal inflammatory process. The adhesion is a condensation of the mesentery that anchors the spleen and upper pole of the kidney to the diaphragm and lateral abdominal wall. This adhesion is avascular, and its release initiates release of Gerota's fascia from the spleen, diaphragm, and anterior abdominal wall (see Figure 2.3). The colon appears to cover more of the surface area of the anterior portion of the kidney on the left side than on the right side.

Medial mobilization of the descending colon allows access to the plane between Gerota's fascia and the colonic mesentery. This natural plane between the mesentery of the descending colon and Gerota's fascia is most easily identified and entered along the lower pole of the kidney or just inferior to the kidney. The anterior and superior aspect of Gerota's fascia is attached to the spleen by the splenocolic ligament, which can be incised in order to fully mobilize the descending colon medially. Typically, release of the splenocolic ligament and medial mobilization of colon off of Gerota's fascia will result in medial mobilization of the tail of the pancreas (see Figure 2.3). Occasionally, however, the tail of the pancreas will remain adherent to the medial surface of Gerota's fascia. As it is not commonly identified during renal surgery, the tail of the pancreas may be mistaken for other structures such as reactive lymph nodes. The pancreas has a characteristic pale lobulated appearance that should be recognized by the urologic surgeon.

Medial mobilization of the descending colon and its mesentery inferiorly results in exposure of the psoas major muscle. Usually, the gonadal vein is identified along the medial aspect of the psoas major muscle (see Figures 2.4 and 2.5). On the left side, the gonadal vein is a very useful landmark because it enters directly into the left renal vein. The gonadal vein can most easily be exposed inferiorly; it is then traced up to its entry into the renal vein. If necessary, for very challenging dissections, the surgeon can carry the dissection down to the level of the inguinal ring in order to reliably identify the gonadal vein and trace it cephalad; this maneuver is particularly helpful in the morbidly obese patient with a large amount of retroperitoneal fat. Anteriorly, along the gonadal vein, there are invariably no tributaries so the surgeon has a safe plane of dissection all the way up to the insertion of the gonadal vein into the main renal vein. Once the gonadal vein has been identified, the ureter can usually be located, as it lies just posterior and lateral to the gonadal vein.

Tracing the gonadal vein cephalad reliably leads to its junction with the left renal vein (see Figures 2.4 and 2.5). It is much more challenging to control the renal vein on the left than the one on the right. Typically, the left renal vein has tributaries, including the gonadal vein inferiorly, one or more posterior lumbar veins that may enter the renal vein posteriorly, and the adrenal vein, which enters the superior edge of the renal vein medial to the insertion of the gonadal vein. Lumbar veins are short and easily disrupted. The lumbar veins may enter the renal vein directly posteriorly or may even join the gonadal vein near its insertion into the renal vein.

Inferior retraction of the superior border of the renal vein will usually expose the renal artery posteriorly. The left renal artery, similar to the one on the right, may lie immediately posterior, slightly cephalad, or slightly caudal to the renal vein (see Figure 2.5). Although dissection of the renal vein usually allows for rapid identification of the

renal artery, preoperative imaging frequently is helpful in challenging cases for discerning the location of the renal artery relative to the renal vein. 'Fortunate' identification of the renal artery anterior to the renal vein should engender much suspicion on the part of the surgeon. Most likely, the arterial structure anterior to the left renal vein is the superior mesenteric artery (see Figure 2.5). This artery must be preserved during renal procedures as its sacrifice results in bowel ischemia. The adrenal gland is located just cephalad to the renal vein. The anatomy of the left adrenal gland is further described later in this chapter. As with the right kidney, there are only flimsy attachments between the posterior aspect of Gerota's fascia and the psoas and quadratus lumborum muscles.

## **Adrenal glands**

### *Overview*

The adrenal glands, like the kidneys, are paired retroperitoneal organs enveloped in Gerota's fascia and surrounded by perirenal adipose tissue. Adult adrenal glands weigh 4–8 g and on average are larger in women than in men. The adrenals lie superior to the kidneys and thus are sometimes referred as suprarenal glands. A layer of loose connective tissue stroma surrounds each gland and separates the adrenal capsule from its respective kidney. Embryologically, the adrenal and kidney develop separately, and if the kidney is ectopic or absent, the adrenal will be in the normal anatomic location. Occasionally, the adrenal gland will be fused with the kidney such that differentiation is difficult and can even be mistaken for a renal tumor.<sup>10</sup> Adrenalectomy for a fused gland may even require a partial nephrectomy.

The three classic layers of the cortex and their respective volumes are the outer zona glomerulosa (15%), the middle zona fasciculata (78%), and the inner zona reticularis (7%). Several steroids are produced from the adrenal cortex, but only a few are biologically active and clinically significant. Aldosterone is produced in the zona glomerulosa, while cortisol and corticosterone are produced in the zona fasciculata. The innermost zona reticularis produces the weak androgen dehydroepiandrosterone (DHEA) and some small amounts of glucocorticoids and estrogens.

The inner medulla is of neuroendocrine derivation. The medulla is derived from the ectodermal neural crest cells in the thoracic region. There is a migration ventrally around the developing aorta and adrenal vein. A group of these chromaffin cells invade the adrenal cortex and eventually are completely surrounded. Preganglionic sympathetic fibers synapse directly to these chromaffin cells, which form the adrenal medulla. Additional developing neuroblasts form the aortic glands or the glands of Zuckerkandl. The glands of Zuckerkandl have no known function, are located laterally to the aorta at the level of the inferior mesenteric artery, and may be a site for extra-adrenal pheochromocytoma (paraganglioma) or neuroblastoma. The chromaffin cells of the adrenal medulla synthesize epinephrine, norepinephrine and dopamine in conjunction with the sympathetic nervous system.

Per gram of tissue, the adrenal receives one of the greatest percentages of cardiac output. The vasculature of the adrenals is split into the multi-vessel arterial system and a



single large vein. The adrenal arteries are divided into three general sources: superior, medial, and inferior branches. The superior supply usually arises from the inferior diaphragmatic artery bilaterally; it is a small plexus of arteries that is difficult to visualize directly. The middle adrenal artery can arise from the aorta, renal artery, or the celiac trunk on the right. The inferior artery usually arises from the renal artery, an accessory renal artery, superior polar renal artery, or small branches from the upper ureteric arteries. There is an abundant branching of the adrenal arteries, leading to up to 50 small perforating vessels over the surface of the capsule. Adrenal venous drainage does not accompany the arterial supply.

The adrenals are true retroperitoneal organs that may be accessed both transperitoneally and retroperitoneally. The retroperitoneal approach is ideal for small tumor burdens such as adenomas. The transperitoneal approach, which may be more familiar to surgeons, is favored for larger pathologic glands such as large adenomas, pheochromocytomas and adrenocortical carcinomas, which may invade adjacent structures. Minimally invasive laparoscopic adrenalectomy has become the true gold standard approach since first performed by Gagner<sup>11</sup> and will be discussed in greater detail in Chapter 49.

### *Right adrenal gland*

Transperitoneal access to the right adrenal begins with a similar previously described dissection of the right kidney. Once the colon is reflected and the duodenum is kocherized, the inferior vena cava is identified. Following the vena cava superiorly leads to the gonadal vein insertion, which is just above the right renal vein. When the lateral border of the vena cava is followed, the main right adrenal vein can be bluntly dissected and visualized. It is a short wide vein found just superior to the renal vein, with an occasional accessory vein entering the inferior phrenic vein. This single, large vein, usually emerging from the adrenal hilum, is a very important surgical landmark. This right vein usually passes obliquely to open posteriorly and drain directly into the vena cava. Damage to this vessel is perhaps the greatest source of vascular injury in right-sided renal and adrenal surgery. The adrenal arterial supply is multifaceted, as previously described. The arterial plexus is usually not clearly visualized but should be considered and handled with either clips or harmonic scalpel.

Once the vasculature is handled, the plane between the adrenal and kidney can be established. The right adrenal is a triangular suprarenal gland with its anterior surface interfacing with the liver, its posterior surface lying on the diaphragm and inferiorly lying on the upper pole of the kidney. The right adrenal is usually engulfed in Gerota's fascia and sandwiched medial to the upper pole of the kidney and lateral to vena cava (see Figure 2.4). The distinctive yellowish-gold tissue of the adrenal stands out even amidst the perirenal adipose tissue.

### *Left adrenal gland*

Transperitoneal access to the left adrenal once again follows access to the kidney. Medial mobilization of the colon is followed by blunt dissection of the renal vasculature. The spleen will completely fall away from the kidney when excised from its previously

described lateral peritoneal attachments in addition to the separation of the splenorenal ligaments. The tail of the pancreas is near in proximity and will be identified at this point. The plane between the pancreatic tail and medial border of the adrenal is separated by mobilizing the left colon mesentery off of Gerota's fascia. Careful exposure of the long left renal vein is the key to the adrenal identification. The left adrenal vein, similar to the gonadal vein, drains directly into the left renal vein and is significantly longer than the right. The left adrenal vein exits the adrenal hilum inferiorly and passes over the anterior surface of the gland, merging with the inferior phrenic vein before entering the renal vein. The adrenal vein enters the renal vein on the superior aspect of the renal vein and medial to the gonadal vein (see Figures 2.4 and 2.5). The left adrenal vein is a crucial landmark for left adrenal surgery and once ligated may be used to identify the gland. Once this long vein is controlled and ligated, medial retraction will create a plane between the adrenal gland and kidney. The left adrenal gland is usually smaller than the right and interfaces with the stomach and pancreas anteriorly, the spleen superiorly, the diaphragm posteriorly, and the upper pole of the kidney inferiorly. The left adrenal gland is identified within Gerota's fascia and more superior to the kidney than its right counterpart. Once again the arterial anatomy is usually not clearly visualized, even with laparoscopic magnification.

## Ureters

### Overview

The ureters are paired muscular urinary conduits that travel from the kidney to the bladder and lie entirely in the retroperitoneal space. The ureter is described radiologically as three segments: *upper* (renal pelvis to upper border of sacrum); *middle* (down to lower border of sacrum); and *lower* or *pelvic* (extends to the bladder). From a surgical standpoint, the ureters are distinguished as the ureteropelvic junction, intermediate tract, and the ureterovesical junction. The ureters are tubular organs and are approximately 22–32 cm in length, varying directly with patient height and renal location. The average diameter of the ureter is 10 mm in the abdominal location and tapers to 5 mm in the pelvis. Microscopically, they are composed of three distinct layers (from outside to inside): the adventitial surface, the muscularis, and the internal uroepithelium. The adventitia consists of a dense network of collagen and elastic fibers in which course the vasculature and neural supply. This layer is continuous proximally with the renal pelvic capsule and distally with the fibrinous tissue known as Waldeyer's sheath. The muscular layer is contiguous with the renal collecting system and bladder.

As a tubular extension of the renal pelvis, the ureter forms a gentle 'S' pattern from the kidney to the bladder. The ureters course along the anterior-medial surface of the psoas muscle embedded in a subserous fascia before encountering the genitofemoral nerve around the 4th lumbar vertebral body (see Figure 2.4). The gonadal vessels cross over the ureter from medial to lateral as the ureter enters the bony pelvis. The ureter continues toward the pelvic brim, turning medial to traverse over the external iliac vessels on the right and the common iliac vessel on the left. In the pelvis it courses medially and

posteriorly to the medial umbilical ligament and enters the detrusor muscle just behind the superior vesicle artery.

### *Vasculature*

The ureter receives its multiple and variable blood supply in a segmental distribution, depending on its level (see Figure 2.5). From proximal to distal, the ureter receives vascular branches from the renal artery, gonadal artery, abdominal aorta, and common iliac artery and, finally, branches of the internal iliac artery. The iliac region of the ureter has the fewest direct arterial branches. The feeding arterial branches approach the ureter medially in the upper ureter and laterally after crossing the iliac vessels in the pelvis. Surgically, it is important to be aware of the apparent vascular course to the affected ureteral segment. Laparoscopic or endoscopic intervention should be limited to the contralateral area (i.e. lateral in the upper ureter and medial in the lower ureter). On reaching the ureter, the perpendicular arterial vessels turn and course longitudinally within the periureteral adventitia as an extensive plexus. Venous drainage follows the arterial supply.

### *Access*

Access to the ureter depends on the affected area (proximal or distal location). Access is generally similar to the lower pole kidney dissection, as previously described. From the transperitoneal perspective, the ureter is identified just posterior to the colon after it is reflected medially and courses along the psoas muscle. The ureter is usually intimately associated with the peritoneum and may at times be reflected with the colon. From the retroperitoneal approach, after balloon dilation, the ureter is located attached to the posterior aspect of the peritoneum and freed off the psoas muscle.

### *Right ureter*

Transperitoneal access to the right ureter follows the steps of renal access, as previously described. Reflection of the right colon and blunt dissection off the lower pole of the kidney is an ideal way to identify the abdominal ureter. Through the retroperitoneal adipose tissue, a gentle sweeping motion of a blunt instrument may initiate ureteral peristalsis. The right ureter leaves the renal pelvis and passes posterior to the second part of the duodenum, running along the lateral aspect of the inferior vena cava. A Kocher maneuver is necessary to access the upper ureter in a non-hydronephrotic system. At this point, the ureter encounters the gonadal vessel as it enters the inferior vena cava. The gonadal vein travels medial and parallel to the ureter, then crosses over and lateral to the gonadal vein. The right ureter descends towards the pelvis and is crossed by the right colic and ileocolic vessels. The right ureter is anteriorly associated with the terminal ileum, cecum, appendix, and the ascending colon. Transperitoneal right ureteral access can be complicated by adhesions from an earlier appendectomy or chronic appendicitis that makes the usually distinct planes difficult to find. A prior appendectomy or history of appendicitis may have caused variations in appendiceal/cecal vascular supplies,

potentially leading to ischemia and secondary bowel perforation from vigorous colonic mobilization. Thus, caution must be exercised when performing the above maneuver.

### *Left ureter*

The left ureter leaves the renal pelvis, running lateral to the aorta and passing behind the left colic vessels. As with the right ureter, the left ureter runs parallel with and lateral to its respective gonadal vein and both pass under the pelvic mesocolon. The left ureter is anteriorly associated with the descending and sigmoid colons.

Important structures near the distal ureter in the male include the vas deferens, which crosses over the distal ureter medial to the middle and upper seminal vesicle before entering the urinary bladder. This is well-visualized transperitoneally in laparoscopic seminal vesicle surgery. In the female, the ureter traverses the posterior aspect of the ovarian fossa, then goes under the inferior part of the broad ligament lateral to the cervix. The uterine artery crosses over the juxtavesical portion of the ureter before it enters the urinary bladder. This becomes a common area of ureteral injury during emergent or radical hysterectomies. Access to the pelvic ureter may require that these structures be identified and divided.

### **Pathology**

The ureters are small tubular organs that can be misidentified in pathologic or even non-pathologic conditions. Midline retroperitoneal masses, such as massive lymphadenopathy, aortic aneurysms, or sarcomas, may laterally deviate the ureters. The disease process of retroperitoneal fibrosis or post-chemotherapy tumors may contract and pull the ureters medially. Several other pathologic entities, such as ureteropelvic junction obstruction or a circumcaval ureter that may lead to hydronephrosis, are associated deviations from normal anatomy.

### **Ureteropelvic junction obstruction**

Accessory crossing arterial and venous vessels contribute to secondary ureteropelvic junction (UPJ) obstructions. Crossing vessels are a significant cause of UPJ obstruction and are more frequently the source in adolescents and adults than in the pediatric age group. An anterior crossing vessel may cause UPJ obstruction in between 25 and 67% of cases and may lead to a failed endopyelotomy or, worse, hemorrhage.<sup>12,13</sup> Because arterial crossing vessels supply the lower pole of the kidney as end vessels, they must be preserved at all costs. Venous vessels may be solitary or run parallel to an artery and may be sacrificed, but ureteroplasty should also be performed in addition to focal upper ureterolysis.

### **Circumcaval ureter**

Circumcaval (or retrocaval) ureter is a rare embryologic condition found on the right side. An anomalous embryologic development of the inferior vena cava (IVC) results in circumcaval ureter. The lack of regression of the fetal posterior cardinal vein causes the

IVC to develop anterior to the ureter and displace it medially. If this obstruction is below the 3rd lumbar vertebrae, the result is ureter obstructed by kinking. The overall incidence is *unknown* and is not symptomatic in every case. Contemporary diagnosis is usually based on three-dimensional volume rendering computed tomography (3D-CT) with intra-venous contrast and diuretic radionucleotide renography.<sup>14</sup>

Indications for reconstruction of the circumcaval ureter include recurrent infection, obstruction, and flank pain. The course of the right ureter is deviated immediately medial to the UPJ, passing posterior to the vena cava before swinging laterally over the vena cava and coursing down toward the urinary bladder. A procedure similar to a dismembered pyeloplasty is used to correct this congenital anomaly.

### **Retroperitoneal fibrosis**

Retroperitoneal fibrosis or Ormand's disease is a nonmalignant inflammatory condition that encases the ureters and great vessels. Retroperitoneal fibrosis has been linked to the migraine medication methysergide or may develop iatrogenically. The fibrous encasement of the ureter may lead to a physiologic obstruction of the ureters by inhibiting peristalsis. The resulting inhibition of peri-stalsis leads to obstruction, which in turn leads to hydronephrosis, pain, and deterioration of renal function. Computed tomography showing a retroperitoneal mass engulfing the retroperitoneal organs routinely makes diagnosis. The radiographic hallmark of this process on intra-venous urography (IVU) or retrograde ureteropyelography (RUPG) is hydronephrosis without ureteral dilation, and severe deviation of the mid-ureters towards the midline. No intrinsic obstructive process is noted on RUPG, and stent placement is easily performed without the need for ureteral dilation. There are reports of unilateral fibrosis, but this should be considered a bilateral process. Secondary retroperitoneal fibrosis may be caused by inflammatory bowel disease, endometriosis, radiation therapy, or post-chemotherapy changes. Bilateral ureteral lysis is curative, but must be coupled with a biopsy of the fibrosis tissue to rule out malignancy.

### **Retroperitoneal lymph nodes**

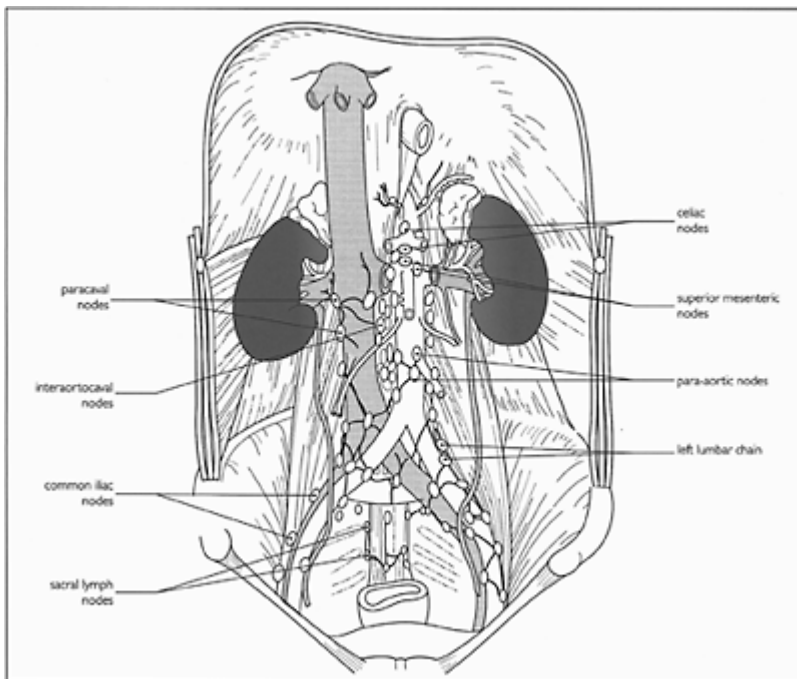
#### *Overview*

Clinically, retroperitoneal lymph node anatomy is important for oncologic surgery. Testicular carcinoma is the one true urologic oncologic disease in which a retroperitoneal lymph node dissection (RPLND) is curative as well as important in diagnostic staging for additional medical therapy. There continues to be a debate whether extended node dissection with radical nephrectomy is necessary because of the poor prognosis when local lymph nodes are involved with cancer. The testes embryologically develop as retroperitoneal organs before their descent. Thus, they obtain their blood supply and lymphatic drainage from the retroperitoneal vascular structure. A clear knowledge of lymph node anatomy is mandatory before contemplating laparoscopic or open RPLND surgery. The spermatic cord carries all of the vascular and lymphatic structures of the testis through the inguinal canal deep to the peritoneum from its origin at the

retroperitoneal vessels. The retroperitoneal lymph nodes can be divided into three major groupings. The main retroperitoneal lymph node chains are named by their relationship to the great vessels (Figure 2.6). The left para-aortic nodes extend from the left ureter to the midline of the aorta. The right paracaval nodes extend from the right ureter to the midline of the inferior vena cava. The remaining nodes, extending from the midline of the aorta to the midline of the inferior vena cava, are called the interaortocaval nodes.

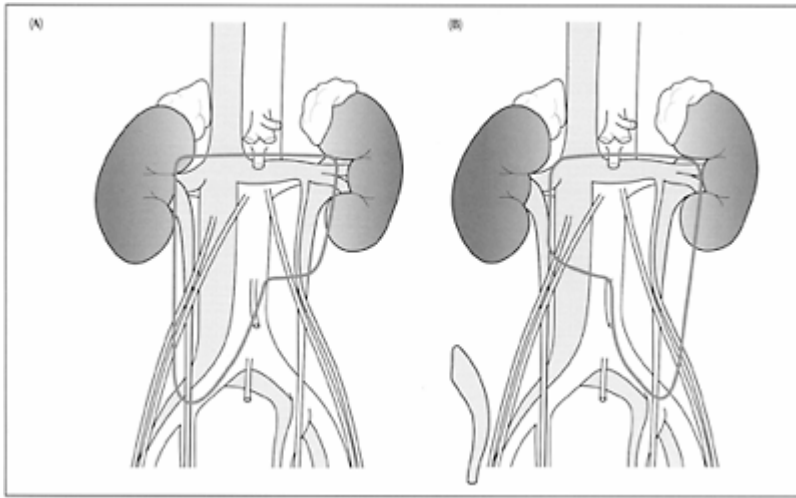
From the observations of Donahue et al, the retroperitoneal drainage of each testis has been mapped.<sup>15</sup> The right testis drains predominantly to the interaortocaval nodes, with significant drainage to the paracaval nodes below the renal hilum. There is a small but significant number of early metastases to the left para-aortic nodes. The left testis drains predominantly to the para-aortic nodes (including nodal tissue above the renal hilum) and there is some significant drainage to the interaortocaval nodes. In the left side, unlike the right side, there is relatively no drainage or associated early metastases in the paracaval region.

With this knowledge, modified RPLND templates have been determined to spare the morbidity of bilateral sympathetic nerve damage (Figure 2.7). Sparing one of the sympathetic chains allows unilateral innervation for the preservation of competent ejaculatory function. Damage to both the right and left sympathetic chains may lead



**Figure 2.6** Retroperitoneal lymph node chains: paracaval (PC),

interaortocaval (IAC), and para-aortic (PA).



**Figure 2.7** Left (A) and right (B) modified RPLND templates.

to retrograde ejaculation and secondary infertility. In template dissections, the lateral border consists of the ipsilateral ureter, superior border, the ipsilateral renal vein, and the inferior margin, the end of the ipsilateral spermatic cord, and the bifurcation of the common iliac artery on the contralateral side.

#### *Right access*

Retroperitoneal node dissection is best approached through a transperitoneal route. The patient should be in left lateral decubitus 45° to facilitate the gravitational retraction and allow access to the entire abdomen for possible open conversion. Extended mobilization of the right and transverse colons should be paramount as the initial approach to the nodal tissue. Freeing the hepatic flexure must not be limited and should include dissection medially and superiorly along the mesenteric root to the ligament of Treitz. The cecum should be mobilized, more extensively than in renal/ureteral surgery. The template borders, as described above, should all be dissected and identified. The right renal hilum should be first evaluated with dissection of the renal vein and ureter after the duodenum is medially relocated (Kocher). The left renal vein is located superiorly to the right vein and should be dissected as laterally as possible. The traditional 'split & roll' technique should start on the vena cava. The origin of the right gonadal vein is carefully identified and ligated. In inflammatory conditions such as enlarged adenopathy or post-chemotherapy situations, the gonadal vein can be identified medial to the ureter at the level of the lower pole of the kidney and followed cephalad. Mobilizing the nodal tissue

laterally frees up the vena cava for the interaortocaval dissection. There are small perforating veins draining the lymphatics encountered at this point. The true right template may be limited medially if the right and transverse colonic attachments have not been mobilized sufficiently. The interaortocaval dissection is extended caudal and to the right of the inferior mesenteric artery, ending inferiorly at the iliac bifurcation on the right.

### *Left access*

Starting with the patient in a 45° right lateral decubitus position, the transperitoneal approach once again mimics extended access to the kidney. The left colon and splenic flexure should be adequately mobilized, allowing complete access to the medial aspect of the aorta. The tail of the pancreas is seen near the medial portion of the upper pole of the left kidney, and blunt dissection medially will facilitate cephalad template dissection. The long left renal vein can be followed to the vena cava and defines the upper template limits. The lateral ureter margin can be identified sitting on the psoas muscle. Once again the lateral nodal packet should be dissected first (para-aortic chain). The ligation of the left gonadal insertion on the inferior location of the renal vein is a good starting place. Once again, the caudal limit is the iliac bifurcation, and the inferior mesentery artery is the marker for bilateral node dissection. Staying on the ipsilateral side of the inferior mesenteric limits the potential of harming both of the sympathetic chains.

## **Pelvic lymph nodes**

### *Introduction*

The initial use of prostate-specific antigen (PSA) as an adjunct for screening resulted in an increased detection of prostate cancer. Since the late 1980s the majority of patients with clinically diagnosed prostate cancer have had stage T1c disease. Prior to PSA and use of clinical staging nomograms, the lack of epidemiologic, radiologic, or physical evidence made the diagnosis of metastatic disease a difficult task. Despite significant refinements in the anatomic approach to the radical retropubic or perineal prostatectomy, they both remain operative procedures with significant morbidity. Radiation modalities have also improved over time with conformal external beam and interstitial brachytherapy delivering lethal doses to the cancer with decreased morbidity to the surrounding structures. Postoperative complications of radical prostatectomy and radiation include urinary incontinence, erectile dysfunction, and fecal incontinence. This significant morbidity mandates that a conservative approach be entertained when a patient is suspected of having metastatic disease. Therefore, one of the goals of laparoscopic pelvic lymphadenectomy (laparoscopic pelvic lymph node dissection) is to exclude select high-risk patients with positive pelvic lymph nodal involvement from non-curative local regional therapy.

Since the establishment of LPLND as a viable procedure in patients with documented prostate cancer, the indications have broadened to include bladder malignancies, penile cancer and urethral cancer. The refinement of equipment and the increasing number of

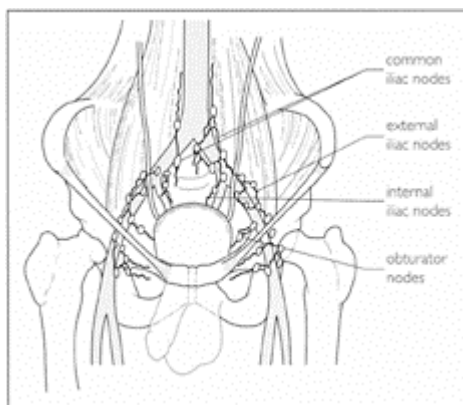


laparoscopically trained surgeons make this minimally invasive approach to staging pelvic lymphadenectomy ideal for suspect patients prior to definitive regional therapy. The combination of a decade of widespread PSA screening and better definitions of the risks of metastatic disease have led to a dramatic decline of stage migration and a decline for LPLND prior to definitive treatment. The increased laparoscopic skills of the urologist and the acceptance of laparoscopic radical prostatectomy will drive a resurgence of LPLND being performed at the same time.

There are several groups of pelvic lymph nodes located around the iliac artery and vein. There are usually 4–6 common iliac nodes located up to the bifurcation. The external iliac nodes are a group of 8–10 nodes located laterally, medially and, occasionally, anteriorly. The internal iliac nodes surround the artery and are a group of 2–4 nodes (Figure 2.8). The obturator lymph nodes are the ones most commonly dissected for prostate cancer. These are considered to be the initial source for lymphatic drainage of the prostate. These are one or two nodes located in the obturator foramen under the external iliac vein and in close proximity to the obturator neurovascular bundle. Lymphatic dissection should be concentrated on the group of nodes associated with the offending cancerous organ. Extended pelvic node dissection can be performed for bladder, penile, and proximal urethral carcinoma.

### *Access*

The approach for pelvic node dissection can be via a transperitoneal or extraperitoneal route. The extraperitoneal approach has several advantages. Through a midline anterior approach, both pelvic sites can be dissected without entering the peritoneal compartment. The peri-toneum acts as a bowel retractor, allowing for a more direct approach to the nodal tissue. Another advantage is the familiarity of the extraperitoneal approach to urologists. In



**Figure 2.8** Pelvic lymph node groups.

the transperitoneal approach, the lateral sidewall with iliac vessels is carefully identified and the peritoneum is opened longitudinally and parallel to the iliac artery, allowing

entrance to the extraperitoneal space. Access to either side can be performed by employing midline trocar sites, and the dissection is similar. Open retropubic prostatectomy traditionally involves the extraperitoneal approach and allows access to the nodal tissue up to the iliac bifurcation. Preperitoneal dissection can be performed bluntly, and pulsations of the iliac artery allow a quick localization of the desired target location. The limits of obturator node dissection include the external iliac vein anteriorly, Cooper's ligament inferiorly, the hypogastric artery and pelvic muscular sidewall laterally, and the bifurcation of the common iliac artery cranially. The large external iliac vein is followed caudal to the pubic bone. Circumflex accessory veins can be encountered and are a potential hemorrhage source. Incising the perivenous tissue allows access to the nodal tissue inferior to the vein and superior to the obturator neurovascular bundle. The perforating vascular and small lymphatic supply to the pelvic nodes is anterior and posterior, with few or no attachments medially and laterally. Care must be taken not to injure the large obturator nerve, which serves as the innervation for ipsilateral lower extremity adduction.

### **Urinary bladder**

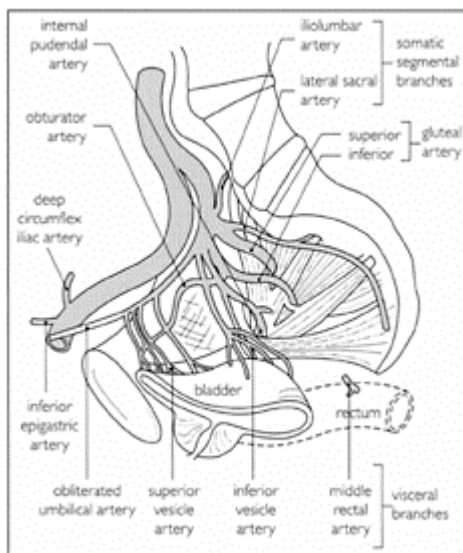
The urinary bladder is perhaps one of the most identifiable extraperitoneal organs. In recent years, laparoscopic cystectomy has established itself as a feasible, minimally invasive approach for oncologic surgery. A purely laparoscopic approach, which includes the urinary diversion, at present, is a lengthy procedure. The combination of laparoscopic cystectomy and extracorporeal reconstructive surgery is an acceptable compromise that allows smaller incisions and a quicker recovery time.

The urinary bladder is a hollow muscular organ whose sole purpose is to act as a reservoir. In simplest terms, the bladder fills over time, stores urine, and empties in a coordinated fashion. When full, the bladder is situated above the pubic ramus, along the anterior abdominal wall, and in severe cases of urinary retention can extend to the umbilicus. As the urinary bladder empties, there is a descent of the bladder dome under the pubic symphysis towards the fixed portion, the trigone. In the female, the superior surface of the bladder is intimately associated with the peritoneum, whereas in the male the entire posterior wall from dome to trigone lies on the peritoneum.

Microscopically, there are distinct layers of the urinary bladder similar to those of the ureter. The watertight uroepithelium is first surrounded by an underlying layer of connective tissue, then bands of linear and circular bands of muscularis, which is covered by a serosal layer. The superior-most area of the bladder, the dome, is attached to the urachal remnant via a short fibrous cord called the urachus. The urachus should be removed en bloc during radical cystectomy because uroepithelial bladder cancer, squamous cell carcinoma, or adenocarcinoma may be present. Urachal adenocarcinoma is a rare malignancy that is often difficult to detect; it should be managed similar to bladder carcinoma.

*Vascular supply*

The internal iliac artery supplies the urinary bladder. Branches of the anterior division of the internal iliac artery include the superior, middle, and inferior vesical arteries. The first branch of the anterior division is one of the main gluteal arteries, which could lead to claudication if inadvertently ligated (Figure 2.9). Small, less-important branches of the obturator, inferior gluteal, and, in the female, uterine and vaginal vessels also contribute to the abundant vascular supply of the urinary bladder. The bladder pedicles approach the bladder from a posterior and lateral approach. A posterior intraperitoneal approach to the bladder results in a delineation of both the lateral and posterior vascular supply, which is easily amenable to ligation using a laparoscopic endo-vascular stapling device.

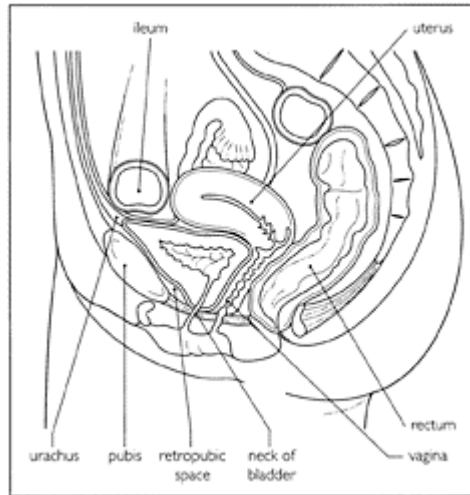


**Figure 2.9** Blood supply of male bladder.

In the male, the bladder extends from the urachus to the dome, then widens to form the bladder proper before funneling and approaching the trigone and bladder neck. The urothelium extends in continuity as the urethra surrounded by the prostate under the pubic bone, then surrounded by corpus spongiosum it traverses the penis. On the superior surface of the male bladder, there is the peritoneal interface and the site for intraperitoneal rupture. Posteriorly, the bladder sits on the peritoneum, which in turn lies on the sigmoid colon and proximal rectum. The ureters enter in a posteriolateral location, being crossed by the ipsilateral vas deferens, prior to becoming transmural. Dissection and clipping of the distal ureter during cystectomy affords direct access to the posterior and lateral bladder vascular pedicles. The vasa deferentia traverse the posterior aspect of the bladder, crossing over the ureter, and then become the ductus deferentes before merging with the base of the seminal vesicles. The ejaculatory ducts exit this junction,

running through the prostate, before becoming the ejaculatory ducts at the verumontanum.

The female bladder has completely different anatomic relationships. The peritoneum interfaces from the bladder dome, down to the posterior wall (Figure 2.10). The reflection of peritoneum interposes between the bladder and uterus and is known as the 'pouch of Douglas'. An anteverted uterus and proximal anterior vagina lie on the posterior bladder wall and therefore are considered part of the radical female cystectomy specimen.



**Figure 2.10** Sagittal section of female pelvis, demonstrating anatomic relation of pelvic structure with the bladder.

### Prostate

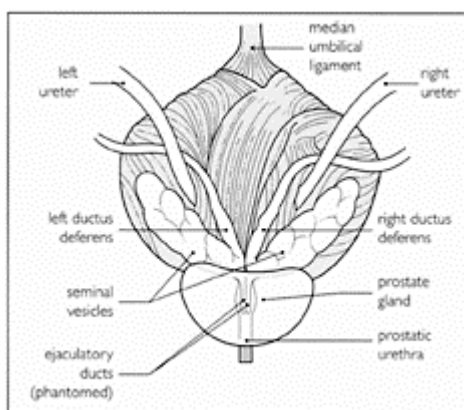
The anatomy of the prostate is surgically challenging because of the position of the gland deep in the pelvis in close proximity to critically important surrounding structures. The rectum, external urethral sphincter, neurovascular bundles, bladder neck, and dorsal venous complex make laparoscopic extirpation of the prostate gland challenging. Although with current technology laparoscopic prostate surgery remains technically demanding, the ability to work in a small space, deep in the pelvis, and with excellent illumination, makes the laparoscopic approach very appealing. The rapid expansion and dissemination of laparoscopic radical prostatectomy is inevitable, but the procedure will require advances in surgical skills and adjunctive technologies, including digital imaging, surgical robotics and, perhaps, anastomotic suturing devices.

Prostatic anatomy has been redefined by the transperitoneal approach to the laparoscopic radical prostatectomy popularized by Guillonnet and Vallancien.<sup>16</sup> The

transperitoneal approach affords the urologist the comfort of familiar anatomic structures and landmarks. When the patient is placed in the Trendelenburg position, the peritoneal contents move cephalad by gravity retraction. Inspection of the operative field will reveal familiar structures anteriorly, including the lateral and medial umbilical ligaments. The urinary bladder is easily identified by locating the Foley catheter in the midline. The internal spermatic rings can be clearly identified with the vas deferens exiting posteromedially and the spermatic vessels entering anterolaterally. Lateral to the medial umbilical ligaments, pulsations of the external iliac arteries can be appreciated through the peritoneum. In thin patients, the outline of the iliac arteries can also be seen. The external iliac veins are usually compressed by standard insufflation pressures, but they are reliably located medial to the external iliac artery.

Using steep Trendelenburg positioning and instrument retraction, the surgeon can identify two pelvic 'arches'. The superficial 'arch' is the transverse vesical fold, and the deep 'arch' is the vesicosacral (sacrogenital) fold. The sigmoid colon can be seen posterior to the lower arch. Incision of the peritoneum just posterior to the deep pelvic arch in the midline will reveal the vas deferens in the midline. Immediately lateral to the vas deferens, the seminal vesicles can be identified with a characteristic white lobular appearance (Figure 2.11). The ureters are located lateral to the seminal vesicles and typically are a more robust tubular structure. If there is any question as to which structure has been identified, the vas deferens can be identified exiting the internal spermatic ring and dissected out to the midline incision.

Cephalad traction on the seminal vesicles and the vas deferens will expose Denonvilliers' fascia. This fascia has a glistening white appearance and can be incised to expose



**Figure 2.11** The posterior view of the bladder and prostate delineating the relationship of seminal vesicles, ureters, and ductus deferentes.

the perirectal fat. Depending on the individual patient's anatomy, the plane between the prostate gland and the rectum sometimes can be developed via this approach. Occasionally, the rectum appears oriented in a more anterior-posterior direction, precluding antegrade dissection to the apex of the prostate. With the transperitoneal approach, the anterior surface of the prostate can only be exposed by mobilizing the bladder. The margins of the bladder are easily identified by instillation of fluid via the Foley catheter. In the midline, the urachus and dome of the bladder are typically more cephalad than is anticipated. Once the bladder has been anteriorly mobilized, the anterior surface of the prostate is easily identifiable. The symphysis pubis is an excellent laparoscopic landmark, as it is quite hard and can easily be appreciated even with the limited tactile sensation afforded by laparoscopic instrumentation.

The endopelvic fascia investing the prostate is covered with a layer of fibroadipose tissue that can be bluntly dissected free and separated from the fascia. Once the fatty tissue is removed, the endopelvic fascia appears white and glistening. Frequently, a small defect in the endopelvic fascia can be appreciated between the lateral aspects of the puboprostatic ligaments and the fascia investing the prostate. Incision of the endopelvic fascia exposes the pubococcygeus component of the levator ani muscle complex laterally and the lateral edge of the prostate medially. In the midline, the superficial dorsal venous veins are relatively subtle because of standard insufflation pressure. The superficial dorsal veins can be controlled easily and safely with bipolar or ultrasonic energy. The branches of the dorsal vein complex are diffuse in their distribution; small branches may pass medially or laterally to the puboprostatic ligaments. The excellent illumination and magnification of laparoscopy allow the laparoscopic surgeon to identify and avoid these structures. In fact, standard insufflation pressures create a tamponade effect and greatly reduce the venous bleeding associated with ligation and transaction of the dorsal vein complex. The urethra lies immediately posterior to the dorsal venous complex. A distinct 'notch' is identifiable as the urethra exits the apex of the prostate. Again, the magnification and decreased bleeding associated with the laparoscopic approach allows for accurate transection of the urethra with preservation of the external urethral sphincter. The rectourethralis muscle connects the posterior aspect of the urethra and the rectum. The fibers of this muscle are distinct and can be transected to separate the posterior aspect of the apex of the prostate and the urethra from the rectum.

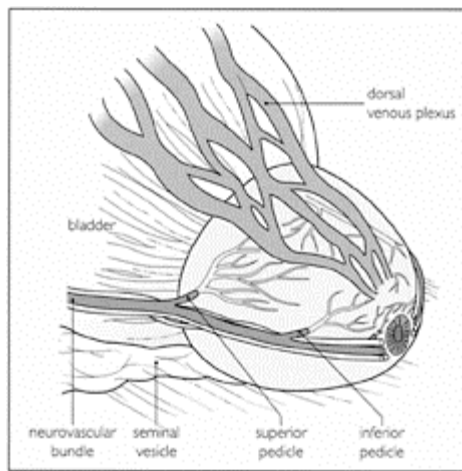
Typically, during open prostate procedures, the bladder anterior neck is identified by palpation. Laparoscopically, the location of the bladder neck can be reliably determined by gently sweeping the fibroadipose tissue off the anterior surface of the prostate in a cephalad direction. At the level of the bladder neck the fatty tissue becomes adherent to the bladder and gives a distinct visual clue as to the location of the bladder neck. Sharp and blunt dissection in the plane between the prostate and bladder neck reveals a relatively avascular plane. Frequently, the urethra can be distinctly identified, and bladder neck preservation is facilitated by the laparoscopic approach. Early retrovesical dissection facilitates transection of the posterior bladder neck as the retrovesical space is easily identified. Anterior traction on the previously dissected vasa deferentia and seminal vesicles allows for posterior dissection of the prostate off the perirectal fat.

The neurovascular bundles may have a variable course but usually are located at the 5 and 7 o'clock positions on the prostate. As the neurovascular bundles run towards the apex of the prostate, their course moves anteriorly. At the apex of the prostate the

neurovascular bundles are located at the 3 and 9 o'clock positions immediately lateral to the urethra (Figure 2.12). Incision of the lateral prostatic fascia and gentle posterior dissection will expose the lateral prostatic pedicle, which can be secured with clips or harmonic scalpel, thus avoiding and preserving the neurovascular bundle.

### Conclusion

Intimate knowledge and thorough understanding of genitourinary anatomy are the foundations of all urologic laparoscopy. This is an enhanced visual approach to anatomic dissection with limited haptic feedback as opposed to open surgery (with its limited visual with full



**Figure 2.12** Superior lateral view of prostate and its neurovascular bundle.

haptic feedback). Thus, laparoscopic visual details of anatomy enables the laparoscopist to approach all urologic disease processes.

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### 3

## Evaluation and perioperative and postoperative care of the endourologic/laparoscopic patient

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Before performing an endourologic or laparoscopic procedure, it is important to evaluate the patient in depth and plan for each stage of their care. This includes preoperative assessment with special attention to comorbidities, close perioperative monitoring in conjunction with anesthesia, and postoperative management according to specific patient needs. This chapter serves as a basic guideline for this planning and provides recommendations for management of patients undergoing minimally invasive surgery.

### **Preoperative evaluation**

#### *History and physical*

The assessment of a patient begins with a thorough history and physical examination. The history should include a history of present illness, comorbidities, past surgeries, social history, medications, and pertinent review of systems. The physical examination should include auscultation of the heart and lungs as well as an inspection for previous surgical scars. A full genitourinary and rectal examination should be performed, and note should be taken of umbilical or inguinal hernias.

#### *Laboratory studies*

Table 3.1 provides general guidelines when choosing preoperative laboratory and radiographic studies. In urologic surgery, baseline creatinine is checked in the majority of patients. Other laboratory values are checked preoperatively before specific operations, e.g. serum prostate-specific antigen (PSA) prior to transurethral resection of the prostate. If the PSA is elevated, a preoperative prostate biopsy should usually be performed. If a patient has diabetes, a fingerstick blood glucose determination should be performed preoperatively and perioperatively. An elevated blood glucose should prompt an investigation for possible infection. A preoperative

**Table 3.1** *Suggested preoperative laboratory and radiographic studies*

| Test                     | Indication  |
|--------------------------|---|
| Complete blood count     | Anticipation of significant blood loss, chronic illness   |
| Electrolytes, creatinine | Renal disease, age >60, diabetes, liver disease   |
| Urinalysis               | Voiding complaints, genitourinary surgery, possible use of prosthetics                              |
| Coagulation studies      | History of bleeding disorder, liver disease, anticoagulant use, family history of bleeding disorder |
| Pregnancy testing        | Any woman of childbearing age   |
| Chest X-ray              | Risk of pulmonary complications, history of pulmonary disease                                       |
| Electrocardiography      | Men>age 40, women>age 50, cardiac history, diabetes   |
| Type+cross/screen        | Anticipation of significant blood loss  |

urinalysis can be helpful prior to endourologic procedures in order to recognize an occult urinary tract infection. A urine culture should be collected prior to an endourologic procedure in patients with chronic catheters in order to give directed antibiotic prophylaxis preoperatively and postoperatively.

### *Medications*

Most medications can be continued perioperatively, exceptions include:

#### **Diabetic medications**

If the diabetes is diet-controlled, no medication changes are necessary. If oral hypoglycemics are being used, they should be held the night before or if long half-life medications are used, e.g. glyburide, they should be held two nights prior to surgery. If the patient is insulin-dependent, half the usual dose of insulin the morning of surgery is usually sufficient.

#### **Anticoagulants**

It is generally accepted that an international normalized ratio (INR) of 1.5 or less is adequate to avoid increased surgical hemorrhage. Preoperative anticoagulation with heparin while warfarin is being held is often necessary in patients with artificial cardiac valves or a diagnosis of deep vein thrombosis (DVT)/pulmonary embolism (PE) within the last month. Warfarin should be held for approximately 4 days prior to surgery and an INR determination can be performed on the day before or the day of surgery. If the INR does not appear to be decreasing in a reasonable amount of time, a small dose of vitamin K (1 mg subcutaneously) may be considered. If intra-venous (IV) heparin is to be used postoperatively, it is often started 12 hours after surgery. Warfarin can routinely be given immediately as it takes several days for its anticoagulant effect to reach therapeutic levels.

With the current patient interest in alternative remedies, a comment should be made concerning the anticoagulant potential of the following medications. Saw palmetto (*Sabal serrulata*) inhibits cyclooxygenase, causing platelet dysfunction and increased bleeding time.<sup>1</sup> Garlic has also been associated with platelet dysfunction and may lead to increased INR in patients taking Coumadin.<sup>2</sup> Therefore, patients should be advised to stop these medications 7 days preoperatively.

Aspirin is an irreversible cyclooxygenase-1 inhibitor and a thromboxane A2 inhibitor. Discontinuation of aspirin at least 7 days prior to surgical procedures allows for new platelet production. Nonsteroidal anti-inflammatory drugs (NSAIDs) are reversible inhibitors of cyclooxygenase and therefore do not have to be stopped as early as does aspirin.

Other antiplatelet agents are not as well studied. Ticlopidine and clopidogrel inhibit ADP-induced platelet aggregation. Manufacturers recommend stopping ticlopidine 10 days and clopidogrel 7 days preoperatively.<sup>3</sup>

### Statins

It is recommended that all HMG-CoA reductase inhibitors (e.g. atorvastatin, simvastatin) be held at least 1 day prior to surgery because of rare case reports of associated perioperative rhabdomyolysis. Some of the cases were severe and resulted in death.<sup>4</sup>

### Bowel preparation and antibiotics

In surgery involving entrance into the bowel or when bowel perforation is considered a significant risk, a full bowel preparation with 4 liters of GoLYTELY solution can be used. In addition, preoperative oral antibiotics to cleanse the bowel contents are often used. One popular antibiotic regimen is 1 g of erythromycin and 1 g of neomycin at 1, 2, and 11 p.m. the day before surgery.<sup>5</sup>

Endourologic procedures are especially high risk for causing bacterial seeding of abnormal or artificial cardiac valves. Ampicillin 2 g IV and gentamicin 1.5 mg/kg IV should be given 30 min prior to surgery. Six hours postoperatively, amoxicillin 1.5 g orally or ampicillin 1 g IV completes the endocarditis prophylaxis. If the patient is allergic to penicillin, vancomycin 1 g IV before surgery and repeated in 8 hours can be used instead of ampicillin/ amoxicillin.<sup>6</sup>

**Radiology** A preoperative chest radiograph can help to discover any pleural or parenchymal abnormality and provides a useful baseline for future postoperative studies. Beyond this, other studies should be performed when indicated, e.g. 3-D computed tomography (CT) when trying to define vasculature before donor nephrectomy or to demonstrate a crossing vessel in ureteropelvic junction obstruction, or magnetic resonance imaging or inferior vena cavagram to image renal tumor thrombus.

*Preoperative risk stratification***Cardiac risk stratification**

Patients and procedures can be separately categorized as either low, intermediate, or high risk. Endourologic procedures are usually felt to be low-risk procedures, except for percutaneous nephrolithotomies, which are low-to-intermediate risk. Laparoscopic cases are considered low- to intermediate-risk procedures. Criteria for patients at increased cardiac risk include:

1. age > 70 years
2. angina
3. prior myocardial infarction (MI)
4. diabetes mellitus
5. history of ventricular ectopy requiring treatment
6. history of congestive heart failure (CHF).<sup>7</sup>

Further major predictors of cardiac risk include:

1. recent MI
2. unstable/severe angina
3. decompensated CHF
4. significant dysrhythmias (high-grade A-V block, symptomatic dysrhythmia, or supraventricular tachy-cardia with uncontrolled ventricular rate)
5. severe valvular disease.<sup>8</sup>

For low- to intermediate-risk procedures, if patients do not have one of the five major predictors of severe cardiac risk, further cardiac testing is not necessary, but if a patient has any of the six criteria for increased cardiac risk, a perioperative  $\beta$ -blocker should be used. ( $\beta$ -blockers have been shown to decrease perioperative MI rates from 18% to 3% in abdominal aortic aneurysm repairs.<sup>9</sup> Postoperative mortality is also decreased in patients using  $\beta$ -blockers, from 14% to 3% in the first postoperative year and from 21% to 10% within 2 years.<sup>10</sup>

**Pulmonary risk stratification**

Laparoscopic procedures with CO<sub>2</sub> gas insufflation place patients with marginal pulmonary function at risk. Pneumoperitoneum places pressure on the diaphragm, causing increased intrathoracic pressure and work of breathing. With insufflation, CO<sub>2</sub> dissolves in the blood-stream and is buffered. When circulating buffers are exhausted, acidosis can be controlled with adequate respiration. If a patient has poor baseline respiratory function, severe acidosis and hypercarbia with possible arrhythmia or effects on various other organ systems can result.

If a patient has severe chronic obstructive pulmonary disease, heavy smoking history, poor activity tolerance, obesity, or neuromuscular/chest wall disease, pulmonary function

tests and a pulmonary medicine consult should be considered. A preoperative arterial blood gas is also helpful to provide a baseline value.

### **Hepatic risk stratification**

Indicators of high surgical risk are severe liver disease, bacterial contamination of ascites, bilirubinemia  $>3$  mg/dl, and albumin level  $<3$  mg/dl. If the patient has a temporary hepatitis, the liver enzymes should be given time to return to normal. If a procedure is considered elective, encephalopathy and ascites should be optimally controlled and nutritional status should be improved as much as possible. When considering laparoscopic surgery, it is important to realize that ascites can cause the intestines to lie closer to the anterior peritoneum, making them more vulnerable to injury when using the Veress needle for access. A Hasson technique should be considered in this situation, and, when closing, the peritoneum should be sutured in a watertight fashion to prevent ascites leak.

### *Contraindications to laparoscopic surgery*

#### **Absolute contraindications**

These include uncorrectable coagulopathy, peritonitis, or malignant ascites.

#### **Relative contraindications**

These include the following:

**Extensive prior surgery or pelvic fibrosis.** From pelvic inflammatory disease, for example, where a Hasson technique to gain access should be considered.

**Organomegaly.** The surgeon should avoid the enlarged viscera or consider a Hasson technique for access.

**Obesity.** In laparoscopy, obesity increases the technical difficulty of a procedure due to instruments being too short, difficulty in maneuvering the instruments with a large layer of subcutaneous fat, and difficulty in defining the internal anatomy as a result of too much peritoneal fat. A multi-institutional study of 125 obese patients undergoing laparoscopic urologic procedures showed that 30% of patients experienced a complication, including 15 patients (12%) who required open conversion.<sup>11</sup>

However, several studies have demonstrated a benefit of laparoscopic vs open surgery in obese patients.<sup>12-16</sup> Forty-two obese patients undergoing renal and adrenal surgery were randomized to laparoscopic or open approaches. The laparoscopic group had longer operating times but had less blood loss (100 vs 350 ml), quicker resumption of oral intake and ambulation (1 vs 5 days), less narcotic requirement (12 vs 279 mg), shorter hospital stay (1 vs 5 days), and quicker convalescence (3 vs 9 weeks). They also found a similar complication rate between the two groups.<sup>12</sup> Doublet and Belair reported on 55 patients undergoing retroperitoneal laparoscopic nephrectomy. The operative time was higher among obese patients (100 min vs 70 min) but otherwise there was a similar complication rate and length of stay between obese and non-obese patients. There were three open conversions in the non-obese patients and none in the obese patients.<sup>13</sup>

A comparison of obese and non-obese patients undergoing laparoscopic donor nephrectomy showed a higher conversion rate for the obese patients but otherwise a similar complication rate and postoperative graft function.<sup>14</sup> Another study included a comparison of 12 obese and 28 non-obese patients undergoing laparoscopic donor nephrectomy. There was no difference between these groups in conversion rate, complications, length of stay, or convalescence.<sup>15</sup> It appears that laparoscopic donor nephrectomy can be carried out safely in obese patients.

### *Contraindications to endoulogic surgery*

#### **Absolute contraindications**

These include uncorrectable coagulopathy, which is an absolute contraindication for percutaneous nephrolithotomy.

#### **Relative contraindications**

These include the following:

**Stone management in pregnancy.** This has been a controversial endourologic topic in recent years. A pregnant woman with flank pain should undergo ultrasound first to check for a stone or hydronephrosis. An intravenous urogram with a single 20 min post-injection film can be performed if additional information is needed.

In the past, stenting the ureter or performing percutaneous nephrostomy during pregnancy was recommended. If a stent or percutaneous nephrostomy is placed, it should usually be changed frequently since encrustation is thought to occur faster in pregnant women. This phenomenon of accelerated encrustation is thought to be due to a combination of hyperuricosuria, absorptive hypercalciuria, and increased incidence of infection during pregnancy.

There are several reports of rigid and flexible ureteroscopy with a combination of stone basketing, holmium laser, pulsed-dye laser, and ultrasonic lithotripsy.<sup>16-25</sup> No obstetric complications except for premature contractions in one patient have been described. In addition, there are reports of encrusted stents being removed using ureteroscopy and one pregnant patient undergoing percutaneous nephrolithotomy for stone disease in the setting of an existing nephrostomy tube.<sup>25</sup> The advantages of ureteroscopy in a pregnant woman include physiologic dilatation of the ureter during pregnancy as well as avoidance of multiple stent or nephrostomy changes.

The theoretical risks of endourologic stone management in pregnant women include premature labor (although no case has yet been reported), transmission of energy to the gravid uterus from laser or other lithotripter devices, and possible release of cyanide as a reaction product during holmium laser lithotripsy of a uric acid stone. Despite these possible risks, the success of multiple reports of ureteroscopy and even percutaneous nephrolithotomy suggest that these approaches are acceptable options in pregnant women.

*Other preoperative considerations***Stent placement**

Ureteral stent placement should be considered preoperatively for easier location of the ureter during laparoscopic surgery.

**Transfusion**

Blood transfusion should be considered in surgical patients preoperatively when the hemoglobin is less than 10 g/dl, especially when significant blood loss is likely. Special consideration should be given to patients with cardiac history, who are at higher risk of adverse events at low hemoglobin levels. Carson et al<sup>26</sup> studied 1958 patients postoperatively who were unable to obtain a blood transfusion for religious reasons. Mortality within 30 days correlated directly with preoperative hemoglobin values, as patients with hemoglobin greater than 12 g/dl had a 1.3% risk of death whereas those with a hemoglobin less than 6 g/dl had a 33.3% risk of death. Patients with a history of cardiovascular disease had an increased risk of death in all hemoglobin categories.<sup>26</sup>

Postoperative transfusion has also been investigated. A total of 838 patients in the intensive care unit were split into two groups. Patients in one group were maintained at a hemoglobin level of 7–9 g/dl and patients in the other group at a hemoglobin level of greater than 10 g/dl. The group maintained at a hemoglobin of 7–9 g/dl had a trend of decreased mortality compared with patients with the higher hemoglobin. This decreased mortality became significant when patients were not critically ill or were less than 55 years old.<sup>27</sup> This study seems to suggest that post-operative blood transfusions should be given only in the setting of ischemic heart disease when patients' hemoglobin values rest in the 7–9 g/dl range. The adverse effects of transfusion may possibly, but not necessarily, be due to increased blood viscosity.

In urologic patients it is recommended that transfusion be used to maintain hemoglobin at 7–8 g/dl except in the case of ischemic heart disease. A cardiac history should prompt an effort to maintain the hemoglobin between 9 and 10 g/dl.<sup>28</sup>

**Antibiotic prophylaxis**

For wound infection prophylaxis, administration of antibiotics 30 min to 2 hours prior to the procedure provides maximum prevention. Additional doses of antibiotics are of no benefit in uncomplicated patients.<sup>29</sup>

For prophylaxis against urinary tract infection (UTI) after endourologic procedures, the recommendations are less strict. There was no difference found in UTI incidence if antibiotics were given 2 hours before or 6 hours after a procedure. Therefore it is acceptable for a patient to take an antibiotic several hours after a cystoscopy is performed in the office.<sup>30</sup> If an endourologic procedure is performed on a patient with an indwelling catheter, special care should be taken to ensure that the patient is on proper antibiotics to target any colonizing organisms. A urine culture is an important part of the preoperative evaluation.

The need for prophylactic antibiotics in percutaneous nephrolithotomy has been investigated.<sup>31,32</sup> In one series, 107 patients were not given any prophylactic antibiotics around the time of their procedure: 35% were found to have postoperative bacteriuria, 10% with temperature  $>38.5^{\circ}\text{C}$ .<sup>31</sup> Another group reported a 2% UTI rate for patients who received antibiotics perioperatively for percutaneous nephrolithotomy vs a 12% rate in patients who had not received antibiotics.<sup>32</sup> Indeed, the evidence seems to suggest that prophylactic antibiotics are indicated for percutaneous nephrolithotomy.

Several studies have addressed the need for prophylactic antibiotics with transurethral resection or cystoscopy.<sup>33-42</sup> Of 1249 patients undergoing urethral manipulation, 5/790 (0.6%) with 3-day prophylactic antibiotics and 16/459 (3.5%) without antibiotics developed a UTI. There was found to be an even greater risk for older patients not using antibiotics.<sup>33</sup> In another study, cefoxitin was administered from the time of surgery until catheter removal (mean 3.8 days) in patients undergoing transurethral resection of the prostate (TURP). At 3 days postoperatively the rate of UTI decreased from 26.4% in a placebo arm to 3.9% and at 7 days postoperatively the rate of UTI decreased from 42% in the placebo to 6.5%.<sup>34</sup> A separate group of patients received nitrofurantoin for 10 days after TURP. The catheters were usually removed 3 days post-operatively and urine cultures collected 24 hours later showed no bacteriuria in patients treated with antibiotics vs a 25% bacteriuria rate in the control group. Furthermore, 47% of controls developed bacteriuria 1 month later vs only 10% of treated patients.<sup>35</sup> Similarly, other studies document an advantage from prophylactic antibiotics in patients undergoing TURP.<sup>36-38</sup> Although one group reported no difference in bacteriuria between patients treated with antibiotics (14%) vs those left untreated (11%), most practitioners believe that the Foley catheter is associated with bacterial colonization and therefore recommend continuing antibiotics until the catheter is removed or resuming antibiotics around the time of Foley catheter removal.<sup>39</sup>

The need for perioperative antibiotics around the time of cystourethroscopy or transurethral resection of bladder tumor (TURBT) is more controversial. Several studies document no advantage to using prophylactic antibiotics with these procedures if no bacteriuria is documented preoperatively.<sup>40-42</sup> Out of 138 patients undergoing outpatient diagnostic cystourethroscopy, 1.5% of those treated with antibiotics and 2.8% left untreated developed bacteriuria.<sup>41</sup> Another group of 30 patients undergoing TURBT were treated with carbenicillin or no antibiotics at all. One patient in the treated group vs no patients in the untreated group developed UTI.<sup>42</sup> It seems that use of prophylactic antibiotics for uncomplicated endoscopic procedures may sometimes be unnecessary; nevertheless, lack of bacteriuria should be documented before choosing to forego antibiotics perioperatively.

The use of antibiotics prior to extracorporeal shock wave lithotripsy (ESWL) has also been evaluated. A meta-analysis involving more than 800 patients demonstrated a reduction in postoperative UTI from 7% to 2% with one dose of prophylactic antibiotics.<sup>43</sup> Therefore, a dose of antibiotics is recommended when performing ESWL. Recommended prophylactic antibiotics for some minimally invasive procedures are listed in Table 3.2.<sup>44</sup>



*Informed consent*

Risks of laparoscopic procedures must be discussed in full, including the possibilities of hemorrhage, infection, bowel injury, death, and any other more specific risks depending on which procedure is to be performed. Also complications unique to laparoscopy should be mentioned, including failure to progress and possible need to convert to open surgery. Medical or other surgical alternatives should also be discussed.

With endoscopic surgery, consent should also involve discussion of risks, including hemorrhage, hematuria, infection, and death, and more procedure-specific risks such as ureteral injury, bladder perforation, or pneumothorax. Open surgery in case of bladder perforation or chest tube placement in case of pneumothorax should be addressed. Possible inability to progress or ureteral injury requiring a stent or percutaneous nephrostomy should be explained as well.

**Table 3.2** *Suggested antibiotics and endourologic procedures*

| Procedure   | Antibiotic   |
|---|--|
| Laparoscopic nephrectomy, adrenalectomy, prostatic brachytherapy  | First-generation cephalosporin. Alternative, penicillinase-resistant penicillin, clindamycin, vancomycin (if MRSA is suspected)                |
| Laparoscopic cystectomy, prostatectomy, ureteral reimplant, nephroureterectomy, pyeloplasty, percutaneous renal surgery | Cephalosporin or ampicillin +/- aminoglycoside, ampicillin-sulbactam. Alternative, levofloxacin, vancomycin/aminoglycoside (if MRSA suspected) |
| Prostate needle biopsy  | Fluoroquinolone  |
| MRSA, methicillin-resistant <i>Staphylococcus aureus</i> .  |  |

### **Postoperative care of the laparoscopic, endourologic patient**

Postoperative care should include resumption of activity within 1 day of surgery and supportive measures, e.g. pain control, IV fluids, when necessary. Specific recommendations concerning nasogastric tubes, nephrostomy tubes, Jackson-Pratt drains, etc., vary with the type and extent of surgery.

With the rapid expansion of laparoscopic capability, more complicated surgeries are being successfully performed. Vigilant postoperative management is essential, and it is important not to discharge patients too soon with the belief that all patients should return home on postoperative day 1 or 2. Vital signs and a physical examination should be performed regularly. Urine output should return to adequate levels postoperatively (>0.5 ml/kg/h) even though intraoperative urine output in laparoscopic surgery is usually decreased, perhaps secondary to decreased renal vein blood flow and direct compression of renal parenchyma.

On discharge, patients should be provided prescriptions for adequate pain medication, stool softener, and antibiotic if indicated. They should be cautioned not to operate a motor vehicle while in significant pain or while using narcotics. Follow-up in the office

should include a woundcheck and review of any pathology results. The section to follow includes some complications occasionally seen during the postoperative period.

### *Other postoperative considerations*

#### **Postoperative myocardial infarction**

Chest pain in association with hypoxia, hypotension, and arrhythmia can suggest an MI or PE. In order to rule out an MI, a daily electrocardiogram (EGG) should be checked for 2 days, a serum troponin I level should be checked every 12 hours for a total of three determinations, and the patient should be moved to a monitored setting. Troponin I levels are more sensitive and specific for detecting MI compared with creatinine phosphokinase.<sup>45</sup> As soon as suspicion is raised for possible MI, the patient should be placed on 2 liters of oxygen and an aspirin should be given, as it has been shown to decrease mortality in acute MI.<sup>46</sup> Furthermore, chest discomfort should be controlled with a combination of narcotics and nitrates, and a cardiology consultation as well as intensive care monitoring should be considered.

#### **Deep vein thrombosis**

Surgical patients are at higher risk for DVT due to the three components of Virchow's triad: stasis, hypercoagulability, and venous injury. Perioperatively, episodes of stasis are common as patients are immobile on the operating room table and on bedrest for the first 1 to 2 days postoperatively. In addition, states of hypercoagulability and increased venous injury may exist due to the release of cellular mediators which affect clotting and the vascular endothelium. If the proper precautions are taken, perioperative DVT has a low incidence (0.8%).<sup>11</sup> In urologic patients, sequential compression devices (SCD) have been recommended for DVT prophylaxis, and it is strongly urged that laparoscopic patients wear SCD perioperatively.<sup>47</sup> Prophylactic doses of heparin or low-molecularweight heparin injected subcutaneously can be considered in patients with additional risk factors, including age >40 years, obesity, malignancy, or previous history of DVT/PE.

Physical examination findings that suggest DVT include unilateral leg edema, erythema, tenderness with dorsiflexion (Homan's sign), or a palpable cord in the groin. A Doppler ultrasound should initially be performed. If the Doppler test is negative or nondiagnostic and suspicion remains high, contrast venography (the radiologic gold standard) may be performed. A diagnosed or highly suspected DVT should be treated with unfractionated IV heparin. Coumadin should be started upon confirmation of the DVT diagnosis, and a goal INR of 2–3 should be targeted. In isolated DVT, subcutaneous injections of lowmolecular-weight heparin can be used while the patient's INR rises to a therapeutic level.<sup>48</sup>

#### **Pulmonary embolism**

Acute onset of chest pain and dyspnea should alert the physician to consider a diagnosis of PE. Diagnostic studies include EGG, which may show right ventricular hypertrophy

with strain, right bundle branch block, and T-wave inversion in leads  $V_1$  and  $V_4$ . Chest radiograph is not a very sensitive test for PE but may demonstrate a Westermarck sign, which appears as decreased peripheral pulmonary vascular markings. An arterial blood gas classically shows a low  $\text{PaO}_2$  and a large A-a gradient. In recent years, helical CT scan with IV contrast has emerged as a sensitive and noninvasive imaging modality for PE. Studies showed 91% sensitivity and 78% specificity for emboli in main pulmonary arteries, but decreased sensitivity (63%) when the emboli were in more peripheral subsegmental arteries.<sup>49,50</sup> If suspicion is high and a helical CT is non-diagnostic, a pulmonary angiogram, the gold standard, may be performed. When IV contrast infusion is contraindicated, a ventilation perfusion scan is an option but is neither as sensitive nor as specific as helical CT. Once PE is discovered, the treatment is similar to that of DVT with IV heparin and long-term anticoagulation using Coumadin. Contrary to DVT management, low-molecular-weight heparin has not been approved for use in PE.

### Conclusions

Successful minimally invasive urologic surgery can provide a patient with multiple benefits compared with an open approach. This success starts with a thorough evaluation of the patient and careful planning of every aspect of the clinical course. Minimally invasive surgeries cannot be treated as procedures without significant risk, and therefore the evaluation and preparation must be complete in order to avoid troublesome results. This chapter aims to provide guidelines for performing successful laparoscopic and endourologic procedures and to facilitate the decision making in the preoperative, perioperative, and post-operative courses.

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## 4

# Endourologic instrumentation and equipment

Michael J Conlin

Endourology is a relatively new urologic field, and it has undergone significant change over the last two decades. Continued improvements in the design and manufacture of endoscopes and working instruments and refinement of our endoscopic techniques have increased the variety of upper urinary tract conditions that can be treated endoscopically. The rapid progress in endoscope and working instrument design can be attributed to significant cooperation between urologists and manufacturers.

Familiarity with available nephroscopes, ureteroscopes, and working instruments can equip the practicing urologist to treat a variety of upper urinary tract problems using minimally invasive techniques.

### **Rigid ureteroscope development**

Hugh Hampton Young first performed rigid ureteroscopy in 1912.<sup>1</sup> During cystoscopy of a 2-month-old child with posterior urethral valves and massively dilated ureters, he was able to pass a 9.5F (French units) pediatric cystoscope through the ureter to the renal pelvis and visualize the calices. Although this was the first ureteroscopy, it wasn't until the late 1970s that Goodman and Lyon separately reported routine rigid ureteroscopy.<sup>2,3</sup> Goodman reported using an 1 IF pediatric cystoscope to perform ureteroscopy in three adults. One of these patients had a distal ureteral tumor which was fulgurated. Lyon et al reported ureteral dilation with Jewett sounds prior to ureteroscopy with an 11F pediatric cystoscope in five adults.

Useful rigid ureteroscopes could not have been developed without the work of Harold Hopkins and his development of the rod lens system in the 1960s.<sup>4</sup> Until then, endoscopic telescopes were manufactured with small lenses separated by relatively large air spaces. The lenses were fragile and could easily become misaligned. The light transmission and optical quality were also poor by modern standards. Hopkins reversed the lenses and air spaces, so the majority of the telescopes were occupied by glass. Glass has a higher refractive index, resulting in better image and light transmission. The smaller air spaces functioned as the lenses. The result was more durable telescopes with improved optical quality and light transmission.

Wolf Medical Instruments developed the first endoscope specifically designed for ureteroscopy in 1979. This 13F endoscope was similar to pediatric cystoscopes, but its longer length (23 cm) permitted further excursion into the ureter of adult men and women.<sup>5</sup> This scope was designed for inspection only, and larger sheaths of 14.5 and 16F were required to perform stone extraction or other therapeutic procedures. These sheaths allowed passage of the relatively limited tools available for stone removal, including

catheters, loops, and baskets. A longer ureteroscope of 39 cm, which could reach the renal pelvis, was developed with Perez-Castro and introduced by Karl Storz in 1980.<sup>6</sup> The longer length permitted inspection of the renal pelvis. Although these early ureteroscopes were useful, they required significant ureteral dilation. Further miniaturization was needed.

Significant advances in fiberoptics led to the development of flexible ureteroscopes, actually prior to routine rigid ureteroscopy. The development of flexible fiberoptics is discussed later in the chapter. Incorporation of fiberoptic image bundles and light bundles into rigid ureteroscopes resulted in smaller ureteroscopes while still maintaining excellent image quality. The first fiberoptic rigid ureteroscope was developed by Candela and reported by Dretler and Cho in 1989.<sup>7</sup> With a tip of 7.2F and two working channels of 2.1F, ureteral dilation was often unnecessary. All modern rigid ureteroscopes incorporate these fiberoptic improvements. Simultaneous improvements in working instruments and lithotripsy devices have made rigid ureteroscopy the standard of care for distal ureteral stones.

### **Characteristics of rigid ureteroscopes**

Although larger rod lens rigid ureteroscopes are available, most endourologists agree that the smaller fiberoptic ureteroscopes are less traumatic, less often require ureteral dilation, and are equally effective. These scopes have tips with diameters of 7F or less, and working channels greater than 3F. Working channels can be larger single or two smaller separate channels. There are significant advantages to having separate working channels. These include the ability to irrigate through one unrestricted channel while a working instrument occupies the other. Separate working channels also permit passage of a lithotripsy device through one channel to fracture a stone that cannot be disengaged from a basket in the other channel. With a single channel this can be difficult because of friction between the two working instruments. Eyepieces are commonly 'in line' with the ureteroscope, which allows



**Figure 4.1** ACMI™ USA Series™ MICRO-6® semi-rigid ureteroscope. (Courtesy of Circon ACMI, Stamford, Connecticut.) Small ureteroscope with two large working channels for diagnostic and therapeutic procedures. It reduces patient trauma and operative time for procedures with minimal or no dilation and general anesthesia. It is also ideal for either laser or electrohydraulic intracorporeal lithotripsy.

easy introduction of the scope (Figure 4.1). Offset eyepiece design (Figure 4.2) permits a straight working channel for the use of more rigid working instruments (such as ultrasonic and pneumatic lithotripsy probes). With the more widespread use of the holmium laser for ureteroscopic lithotripsy, the need for ureteroscopes with offset eyepieces has decreased. Table 4.1 shows the specifications of the currently available fiberoptic rigid ureteroscopes.

Larger ureteroresectoscopes (11.5F) can be useful for large distal ureteral tumor resection (Figure 4.3). Some urologists prefer this instrument for ureteroscopic endopyelotomies.<sup>8</sup> Preoperative ureteral stenting is necessary in this setting to allow passage of the ureteroresectoscope to the ureteropelvic junction.





**Figure 4.2** USA Series™ MRO™-6 MICRO operating ureterscope. (Courtesy of Circon ACMI, Stamford, Connecticut.) The offset eyepiece is designed for physician comfort and the straight working channel gives added control for use of rigid operating instruments such as ultrasonic and pneumatic lithotripsy probes.



**Figure 4.3** Rigid ureteroresectoscope. (Courtesy of Circon ACMI, Stamford, Connecticut.)

**Table 4.1** *Fiberoptic rigid ureteroscopes (data supplied by manufactures)*

| Model  | Eyepiece        | Diameter (F)  | Working length (CM)      | Channels | Channel size (F) | Field of view (degrees) | Angle of view (degrees) | Focusing ocular |
|--|-----------------|---------------|--------------------------|----------|------------------|-------------------------|-------------------------|-----------------|
| <b>Circon ACMI (Stamford, Connecticut)</b>                       |                 |               |                          |          |                  |                         |                         |                 |
| MR6  | Standard        | 6.9/8.3/10.2  | 33 (MR6); 41 (MR6L)      | 2        | 2.3; 3.4         | 65                      | 5                       | Yes             |
| MR9  | Standard        | 9.4/10.2/12.6 | 33 (MR9); 42 (MR9L)      | 2        | 2.1; 5.4         | 65                      | 5                       | Yes             |
| MRO6   | Angled offset   | 6.9/8.3/10.2  | 33 (#633); 42 (#642)     | 2        | 2.3; 3.4         | 65                      | 5                       | Yes             |
| MRO7   | Angled offset   | 7.7/9.2/10.8  | 33 (#733); 42 (#742)     | 1        | 5.4              | 65                      | 5                       | Yes             |
| MRO742-A   | Angled offset   | 7.7/9.2/11.2  | 42                       | 1        | 5.4              | 65                      | 5                       |                 |
| <b>Olympus America (Lake Success, New York)</b>                  |                 |               |                          |          |                  |                         |                         |                 |
| A2940A; A2941A   | Angled          | 6.4/7.8       | 43 (A2940A); 33 (A2941A) | 1        | 4.2              | 88                      | 7                       | No              |
| A2942A   | Angled          | 8.6/9.8       | 43                       | 1        | 6.6              | 88                      | 7                       | No              |
| A2948A; A2949A   | Straight        | 6.4/7.8       | 43 (A2948A); 33 (A2949A) | 1        | 4.2              | 88                      | 7                       | No              |
| <b>Karl Storz Endoscopy (Culver City, California)</b>            |                 |               |                          |          |                  |                         |                         |                 |
| 27400CK/CL   | Movable/angled  | 7.5/9/10.5    | 34 (CK); 43 (CL)         | 2        | 2.4; 3.5         | 80                      | 0                       | Yes             |
| 27410SK/SL   | Straight        | 7.5/9/10.5    | 34 (K); 43 (L)           | 2        | 2.4; 3.5         | 80                      | 0                       | No              |
| 27410CK/CL   | Angled          | 7.5/9/10.5    | 34 (K); 43(L)            | 2        | 2.4; 3.5         | 80                      | 0                       | No              |
| 27430K/L   | Angled          | 8/9/10.5/11   | 34 (K); 43 (L)           | 2        | 2;4              | 80                      | 0                       | No              |
| 27401K/L   | Movable/angled  | 10/10.5/12/13 | 34 (K); 43 (L)           | 2        | 3; 5.5           | 80                      | 0                       | Yes             |
| 27411K/L   | Angled          | 10/10.5/12/13 | 34 (K); 43(L)            | 2        | 3; 5.5           | 80                      | 0                       | No              |
| 27023SA/SB   | Straight        | 10/10.5/12/13 | 34 (SA); 43(SB)          | 2        | 3; 5.5           | 80                      | 0                       | No              |
| <b>Richard Wolf Medical Instruments (Vernon Hills, Illinois)</b> |                 |               |                          |          |                  |                         |                         |                 |
| 8721   | Standard        | 4.5/6         | 31                       | 1        | 2.5×3.6 (oval)   | 73                      | 0                       | No              |
| 8702; 8712   | Standard        | 6/7.5/8.5     | 31 (8702); 42.5 (8712)   | 1        | 4.2×4.6 (oval)   | 73                      | 0                       | No              |
| 8702.523; 8702.524   | Parallel offset | 6/7.5/8.5     | 31.5 (8702.523);         | 1        | 4.2×4.6 (oval)   | 73                      | 0                       | No              |

|                       |          |           |   |                  |                   |          |     |
|-----------------------|----------|-----------|---|------------------|-------------------|----------|-----|
|                       |          |           |   | 43<br>(8702.524) |                   |          |     |
| 8702.533;<br>8702.534 | Angled   | 6/7.5/8.5 | 31.5<br>(8702.533);<br>43<br>(8702.534) | 1                | 4.2×4.7<br>(oval) | 73<br>0  | Yes |
| 8707, 8703            | Standard | 8/9.8     | 31 (8707);<br>42.5 (8703)               | 1                | 5.2×6.2<br>(oval) | 74<br>10 | No  |
| 8705; 8719            | Offset   | 8/9.8     | 31 (8719);<br>42.5 (8705)               | 1                | 5.2×6.2<br>(oval) | 74<br>10 | No  |
| 8704                  | Offset   | 8.5/11.5  | 31                                      | 1                | 6.2×8.2<br>(oval) | 74<br>10 | No  |

### Flexible ureteroscope development

The history of flexible endoscopy is closely tied to the development of flexible fiberoptics. When light travels through a medium such as glass, internal reflection of the light occurs at the interface between that medium and its surroundings. This physical property of internal reflection which allows bending of light within flexible glass was first reported by Tyndall in 1854.<sup>9</sup> This technique of image transmission using internal reflection was patented in 1927. Current medical fiberoptic technology is based upon this physical property first demonstrated nearly 150 years ago.

Molten glass can be drawn or pulled into small-diameter fibers. These fibers will uniformly transmit light from one end to the other proportional to the light input. When the fibers are bundled randomly (such as the 'light bundle' within flexible endoscopes) and connected to a light source, they provide excellent light transmission for illumination. When the fibers are bundled with identical fiber orientation at each end (i.e. coherent), the single dots of light will coalesce to transmit images. 'Cladding' each individual fiber of glass with a second layer of glass of a different refractive index will improve the internal reflection and light transmission. This cladding process was developed and reported by Curtiss and Hirschowitz in 1957.<sup>9</sup> These men later reported the first use of a flexible gastroscope, which was used to visualize a duodenal ulcer. Cladding the fibers also improves the durability of the image bundles. The mesh-like appearance of the image from flexible endoscopes is due to the lack of light transmission through this cladding. The quality of the image obtained depends upon the number of fibers and how closely they are packed within the image bundle. Improvements in image bundle manufacture have allowed closer packing of more fibers, resulting in improved images, smaller outer diameters, and larger working channels in both rigid and flexible endoscopes.

Early flexible ureteroscopy, reported by Marshall in 1964 and later by Takagi et al and Bush et al, actually predated the first reports of routine rigid ureteroscopy.<sup>10-12</sup> Marshall reported passage of a 9F flexible endoscope through a 26F cystoscope into the ureter. A ureteral stone was visualized, but because there was no deflecting mechanism or working channel, little else could be done. These early prototype flexible ureteroscopes could only be used for visualization of the upper urinary tract. Because of these limitations, flexible ureteroscopy did not achieve widespread acceptance.

Takagi and coworkers reported their use of a flexible ureteroscope with deflecting tip allowing visualization of the calyces in 1971.<sup>12</sup> They and other urologists continued to improve flexible ureteroscopic techniques, such as the use of ureteral guide tubes and the use of diuresis for improved visualization. However, the interest of urologists and endoscope manufacturers remained focused on rigid ureteroscopy, and rapid improvements in rigid ureteroscopes dominated the 1980s. Access to much of the upper urinary tract for fragmentation of calculi was possible with these rigid endoscopes. When the limitations of the rigid ureteroscopes became apparent, there was renewed interest in flexible ureteroscope development. The later addition of active deflection, larger working channels, and effective working instruments 3F and less made possible the diagnosis and treatment of many more upper urinary tract problems than was possible with rigid ureteroscopes alone.

### Characteristics of flexible ureteroscopes

The basic components of flexible ureteroscopes include the optical system, deflection mechanism, and working channel (Figure 4.4). The optical system consists of the flexible fiberoptic image and light bundles. Improvements in the image bundles have been discussed in the preceding

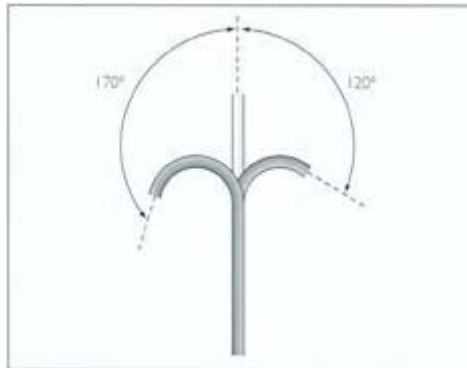


**Figure 4.4** USA Series™ DUR™-8 durable flexible ureteroscope system. (Courtesy of Circon ACMI, Stamford, Connecticut.) A flexible ureteroscope

has a dual deflection that facilitates access to the proximal ureter and the renal pelvis; it allows complete intrarenal access, including the lower pole calyces.

section. Small lenses attached to the proximal and distal ends of the image bundle create a telescope with image magnification, increased field of view, and focusing ability. By changing the axis of the optical system at the tip of the scope, the angle of view of the ureteroscope can be changed to improve early visibility of any working instruments passed out the working channel.<sup>13</sup> Another recent design modification is the splitting of the light bundle distally to provide more than one point of light transmission. This permits a more centrally placed working channel as well as better distribution of the light within the field of view.

The deflection mechanism is an integral part of flexible ureteroscopes (Figure 4.5). It permits complete maneuverability within the intrarenal collecting system.<sup>14</sup> Most deflecting mechanisms consist of control wires running down the length of the ureteroscope attached on the proximal end to a manually operated lever mechanism. Distally, the wires run through movable metal rings to the distal tip where they are fixed. Moving the lever up or down will pull the control wire and move the tip. When the tip moves in the same direction as the lever, the deflection is said to be 'intuitive' (i.e. down is down and up is up). Most modern flexible ureteroscopes allow both up and down deflection in a single plane.<sup>15</sup> This plane of deflection is marked by the reticle seen as a notch within the field of view of the ureteroscope (Figure 4.6). The active deflection mechanism frequently wears out with repeated use, requiring repair. Improvements in the design of the deflecting mechanism with each new generation of flexible ureteroscopes should improve durability.



**Figure 4.5** Flexible uretero-fiberscope. (Courtesy of Olympus America, Lake Success, New York.) The deflection

mechanism is an integral part of a flexible ureteroscope. Active deflection of the ureteroscope allows visualization of the lower pole in most patients.



**Figure 4.6** Endoscopic image of renal stone, guide wire, and laser fiber seen through a flexible ureteroscope. A reticle is seen at 1 o'clock.

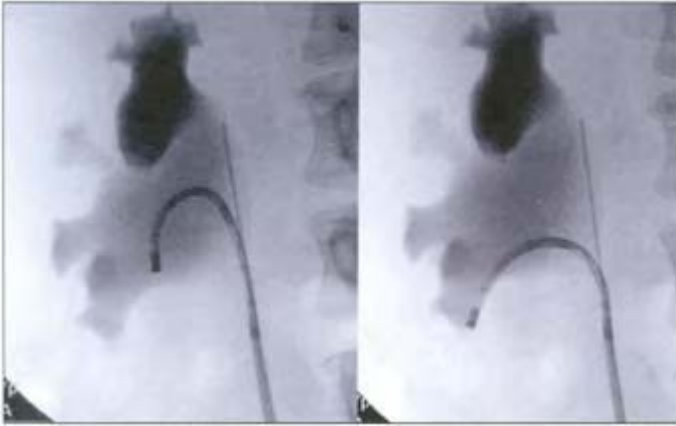
Modern flexible ureteroscopes permit down deflection of approximately  $180^\circ$ . Bagley and Rittenberg measured the angle between the major axis of the ureter and the lower pole infundibulum (ureteroinfundibular angle) in 30 patients.<sup>16</sup> They reported the average angle to be  $140^\circ$ , with a maximum of  $175^\circ$ . Active deflection of the ureteroscope of  $180^\circ$  should allow visualization of the lower pole in most patients. However, reaching into the lower pole calyx with the tip of the ureteroscope can still be difficult. Active deflection occurs only at the distal tip of the ureteroscope, and the deflected segment may not be long enough to reach the lower pole calyx. The secondary, passive deflection mechanism addresses this problem. All flexible ureteroscopes have a more flexible segment of the ureteroscope due to a weakness in the durometer of the sheath, located just proximal to the point of active deflection. By passively bending the tip of the ureteroscope off of the superior margin of the renal pelvis, the point of deflection is moved more proximally on the ureteroscope, effectively extending the tip of the ureteroscope. When passive deflection is used, the lower pole calyx can be reached in over 90% of patients. Significant hydronephrosis can limit the ability to engage passive secondary deflection and reach the lower pole.

The first ureteroscope incorporating active secondary deflection was developed by Circon ACMI (Stamford, Connecticut). In addition to active primary deflection of  $185^{\circ}$  down and  $175^{\circ}$  up, there is a second control lever for active secondary deflection of  $165^{\circ}$  (Figure 4.7). This ureteroscope should enable the urologist to reach the lower pole even under conditions when access with passive secondary deflection is not possible (Figure 4.8).

All currently available flexible ureteroscopes have working channels of at least 3.6F size. This allows use of



**Figure 4.7** USA Series™ DUR™-8 Elite durable flexible ureteroscope system with primary and secondary deflection. (Courtesy of Circon ACMI, Stamford, Connecticut.) This ureteroscope provides an active secondary deflection. In addition to active primary deflection of  $185^{\circ}$  down and  $175^{\circ}$  up, there is a second control level for active secondary deflection of  $165^{\circ}$ .



**Figure 4.8** Inability to access the lower pole with primary deflection (left), but the lower pole is easily accessed using active secondary deflection (right).

instruments up to 3F, while still permitting adequate irrigation. When working instruments are used, higher pressure irrigation will be necessary to compensate for the effectively smaller irrigation channel. This higher pressure irrigation can be delivered using a pressurized irrigation bag, roller pump, or hand-held syringes. The specifications of currently available flexible ureteroscopes are detailed in Table 4.2.

Rigid and especially flexible ureteroscopes are very delicate instruments and need to be handled accordingly. Any damage to the working channel, deflecting mechanism, or fibers within the image bundle can render the ureteroscope useless. Ureteroscopes, including the working channel, should be cleansed with warm water and a nonabrasive detergent after each use. Sterilization of ureteroscopes can be performed by gas (ethylene oxide), soaking in a glutaraldehyde solution, or by using the Steris system (Mentor, Ohio).<sup>17</sup> The Steris system provides automated washing and rinsing of the endoscopes in a peracetic acid solution.

### Nephroscopes

Percutaneous nephrostolithotomy developed from early experience with antegrade pyelography in the early 1950s. Percutaneous nephrostomy was described by Goodwin et al in 1955 for the relief of hydronephrosis.<sup>18</sup> Surgical nephrostomy tube placement was largely replaced by percutaneous nephrostomy placement in the mid 1970s. In 1976, Fernstrom and Johansson placed a nephrostomy tube to remove a renal calculus.<sup>19</sup> It was the refinement of the percutaneous nephrostomy procedure that led to the development of percutaneous nephroscopy and nephrostolithotomy in the 1980s.



Percutaneous nephrostolithotomy is most commonly performed to remove large volumes of stone. Currently,

**Table 4.2** *Flexible ureteroscopes*

| Parameter                                    | Manufacturer/Model |       |                             |                    |         |              |          |
|--|--------------------|-------|-----------------------------|--------------------|---------|--------------|----------|
|  | Circon-ACMI        |       |                             | Olympus Karl Storz |         | Richard Wolf |          |
|  | AUR-7              | DUR-8 | DUR-8 elite                 | URF-P3             | 11274AA | 7330.072     | 7325.172 |
| Tip diameter (F)                             | 7.5                | 6.75  | 6.75                        | 6.9                | 7.5     | 7.4          | 6.8      |
| Shaft diameter (F)                           | 7.5                | 8.6   | 8.6                         | 8.4                | 8.0     | 9.0          | 7.5      |
| Working length (cm)                          | 65                 | 65    | 65                          | 70                 | 70      | 70           | 70       |
| Channel size (F)                             | 3.7                | 3.6   | 3.6                         | 3.6                | 3.6     | 4.5          | 3.6      |
| Active deflection up (degrees)               | 100                | 175   | 175                         | 180                | 120     | 130          | 130      |
| Active deflection down (degrees)             | 160                | 185   | 185                         | 100                | 170     | 160          | 160      |
| Location of passive deflection (cm from tip) | 7.5                | 7.5   | Active secondary deflection | 4.0–7.0            | 5.0     | 6.0          | 6.0      |
| Angle of view (degrees)                      | 0                  | 12    | 12                          | 0                  | 6       | 0            | 0        |
| Field of view (degrees)                      | 80±5               | 80±5  | 80±5                        | 90                 | 90      | 65           | 65       |
| Depth of field (mm)                          | 2–40               | 2–40  | 2–40                        | 1–50               | 2–50    | 2–40         | 2–40     |
| Magnification                                | 30×                | 30×   | 30×                         | 52×                | 40×     | 50×          | 50×      |

the most effective intracorporeal lithotripsy energy for quickly removing large volume of stone is ultrasonic. Rigid nephroscopes are built with this in mind. The ultrasonic lithotripsy probes used for percutaneous applications are 3.5–4 mm in diameter and rigid. The working channels of rigid nephroscopes must be straight and large enough to accommodate these probes. Most rigid nephroscopes use rod lens technology, which provides superior optics. The eyepiece is offset to allow a straight working channel (Figure 4.9). Irrigation delivered through the large working channel is generally excellent, with some nephroscopes incorporating continuous flow designs. Flexible cystoscopes are frequently used as nephroscopes (Figure 4.10). Flexible nephroscopy combined with holmium laser lithotripsy and tipless baskets for fragment removal have decreased the need for multiple percutaneous accesses in most cases.

### Guide wires

Guide wires are essential to endourologic procedures (Figure 4.11). They are used for many portions of these procedures, including establishment of percutaneous access, ureteroscopic access, straightening of the ureter, a guide for dilation of the ureter or percutaneous tract, and for stent placement. There are many different guide wires available, differing in diameter, rigidity, tip design, materials, and coating. The choice of

the most appropriate wire will depend upon the task involved, and the patient's anatomy and upper urinary tract problem being confronted.

The most common guide wire design is a solid core stainless steel wire around which an outer wire is wrapped. Nitinol (nickel-titanium alloy) inner wires give guide wires a kink-resistant construction. Because of nitinol's 'memory' quality, reliable angling of the tip is possible. Many newer wires have a nitinol core wire and a polyurethane outer cover. When coated with a hydrophilic polymer, these exceptionally slippery wires are useful for negotiating around impacted ureteral calculi, tortuous ureters, and ureteral strictures (Figure 4.12). The hydrophilic-coated wires are too slippery to be reliable safety wires, because of their tendency to slide out of the patient. When these wires are used for initial access, they are exchanged for a standard safety wire. New hybrid designs incorporating a hydrophilic tip with a standard Teflon (polytetrafluoroethylene; PTFE)-coated shaft may serve as both the access and safety wires for these difficult access cases.

Guide wires for urology range in diameter from 0.018 to 0.038 inches, the most commonly used being 0.038 inches in diameter. Lengths vary from 80 to 260 cm (centimeters). The most useful length for endourology is 145 cm. The tips



**Figure 4.9** Percutaneous nephroscope. (Courtesy of Olympus America, Lake Success, New York.) The offset eyepiece allows a straight working channel.



**Figure 4.10** USA Series™ ACN™-2 Flexible CystoNephroscope. (Courtesy of Circon ACMI, Stamford, Connecticut.) The flexible nephroscope allows access to the different calyces via one percutaneous site and thus decreases the need for multiple percutaneous accesses in most cases.



**Figure 4.11** Guide wires. (Courtesy of Circon ACMI, Stamford, Connecticut.) Many guide wires are available, differing in diameter, rigidity, tip design, materials, and coating.



**Figure 4.12** Roadrunner PC<sup>®</sup> wire guides with Slipcoat<sup>™</sup> hydrophilic coating. (Courtesy of Cook Urological, Spencer, Indiana.) This guide wire has a nitinol core wire and a polyurethane outer cover coated with a hydrophilic

polymer. This slippery guide wire is very useful for negotiating around impacted ureteral calculi, tortuous ureters, and ureteral strictures.

of these wires are generally 'floppy' for 1–3 cm. Bentson and Newton wire designs have flexible tips of up to 15 cm, and are seldom used today. Some wires have a movable core wire which can be partially withdrawn to increase the length of the flexible tip. Other variable characteristics in guide-wire construction include the distal tip design and the wire stiffness. The distal tip can be straight, angled, or 'J' tipped. The rigidity of the wires can be varied by changing the diameter and design of the inner core wire. Stiffer wires are useful for straightening out tortuous ureters, and dilating long percutaneous tracts in obese patients.

The choice of the most appropriate guide wire for the endourologic task at hand can mean the difference between success and failure. Despite all of these advances in wire design and construction, an 0.038-inch diameter straight, flexible tip, Teflon-coated, stainless steel wire is still the best choice for most cases.

### **Dilation devices**

Ureteral dilation is less necessary for ureteroscopy with the advent of the newer, smaller-diameter ureteroscopes.<sup>20</sup> Ureteral dilation can be accomplished passively with indwelling stent placement. More commonly, ureters are dilated with dilating catheters (Figure 4.13) or balloons (Figure 4.14). Ureteral dilating catheters are hydrophiliccoated polyurethane catheters, tapered from a 6F tip to 12F shaft, and are passed over a wire to dilate the ureter.<sup>21</sup> Ureteral balloon dilators are also passed over a wire, have a low profile of 3–8F, and dilation diameters of 12–30F. Dilation of the ureter beyond 15–18F is rarely necessary for routine ureteroscopy. Balloons can have maximum inflation pressures of 8–20 atmospheres, depending upon the design and the material used for balloon manufacture. Zero-tip design ureteral balloon dilators are useful for dilating immediately adjacent to an impacted ureteral calculus. Ureteroscopic balloon dilators are 3F in size, can be inflated to 12F, and are passed directly through the ureteroscope. They are used to dilate under direct vision such as dilation of stenotic infundibula and calyceal diverticular necks. Once inflated, these ureteroscopic balloons often cannot be removed through the ureteroscope. The ureteroscope must be removed with the balloon.

The most common dilation devices for percutaneous tracts are the disposable Amplatz dilators (Figure 4.15), and balloon dilators (Figure 4.16). The Amplatz dilators are tapered tip catheters sequentially passed over a wire in increasing sizes. The balloon dilation systems are faster and simpler to use and don't require multiple passes over the wire. The Amplatz dilators are better than the balloon dilators for dilating scar tissue from previous renal surgery.



**Figure 4.13** Ureteral dilators. (Courtesy of Cook Urological, Spencer, Indiana.) Dilators are used for dilation of the ureter prior to ureteroscopy and/or stone manipulation.



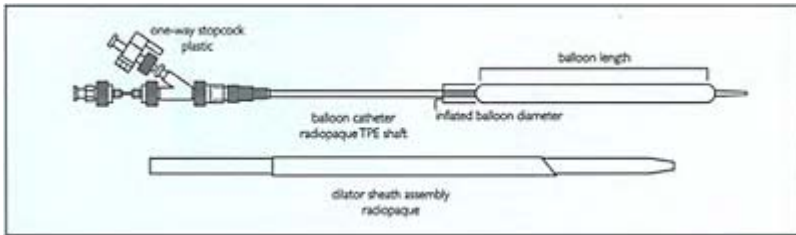
**Figure 4.14** Balloon ureteral dilator. (Courtesy of Cook Urological, Spencer, Indiana.) A ureteral dilation balloon catheter is used for transluminal dilation of ureteral strictures or ureteral dilation prior to ureteroscopy or stone manipulation. It has radiopaque markers that indicate the proximal and distal ends of the balloon.



**Figure 4.15** Amplatz renal dilator set. (Courtesy of Cook Urological, Spencer, Indiana.) This set allows sequential dilation of a tract to the kidney for percutaneous access. The tips of the catheters are tapered to pass over a wire in increasing sizes.

### Stone retrieval devices

Essentially, any working instrument 3F or less in size can be used through the ureteroscope. These include a variety of stone graspers and baskets, electrodes, cup biopsy forceps, and intraluminal lithotripsy devices. Three-pronged stone-grasping forceps are the safest instruments for removing calculi with the flexible ureteroscope (Figure 4.17). They permit disengagement of calculi that have been found to be too large to be safely removed from the ureter. In fact, their grasp is weak enough to release the stone if too much force is applied. This is critical when performing flexible ureteroscopy because there is no second channel to permit fragmentation of an unyielding stone trapped within a basket. Rigid ureteroscopes with two working channels have this added degree of safety, permitting more routine use of baskets. The components of stone baskets include the control handle, the control wire, the sheath, and the basket itself. Stone baskets are available in the usual helical and flat-wire designs, and can also vary in the



**Figure 4.16** Nephrostomy tract dilator set. (Courtesy of Cook Urological, Spencer, Indiana.) The balloon dilator is used to dilate the musculofascial tract, renal capsule and parenchyma during percutaneous procedures. Radiopaque markers are placed at the proximal and distal ends of the balloon. A radiopaque dilator/sheath is fitted to the balloon catheter to allow coaxial placement.



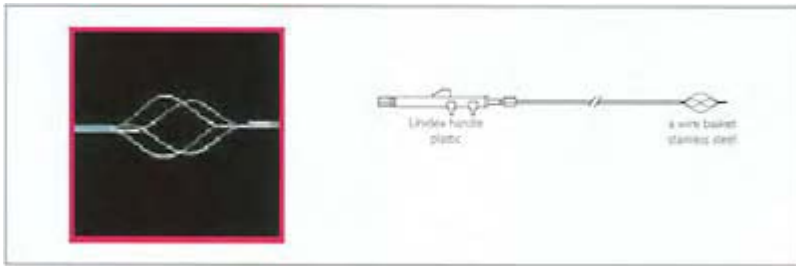
**Figure 4.17** Grasping forceps. (Courtesy of Circon ACMI, Stamford, Connecticut.) A grasping forcep for stone removal with a ureteroscope.

number and type of wires used. Two sheathing materials are available, Teflon and polyimide. Polyimide is a very durable but stiff material and will limit deflection of the flexible ureteroscope. Teflon does not limit deflection as much as polyimide. Newer hybrid designs incorporate Teflon at the tip and polyimide in the shaft, to emphasize the

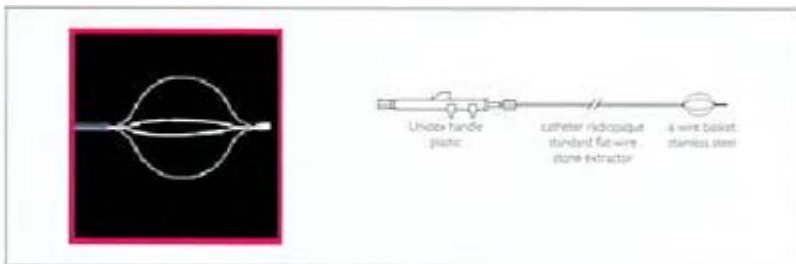


advantages of each material. Helical baskets can be made with three-, four- or double-wire designs with six or more wires (Figure 4.18A,B). The double-wire designs have improved opening strength, which may facilitate removal of impacted calculi. Helical baskets have round wires, and unlike flat-wire baskets, are safe to rotate within the ureter. They are opened above the stone and pulled down while rotating the basket to engage the stone.

Flat-wire baskets are nonhelical and are designed to have larger spaces between the wires to allow engagement of larger stones (Figure 4.19A,B). Most are constructed with four wires. They were originally designed for percutaneous use, where, by filling the calyx when opened, they can more



**Figure 4.18A,B** Helical stone extractor. (Courtesy of Cook Urological, Spencer, Indiana.) Helical baskets are made with three-, four-, or double-wire designs with six or more wires. The double-wire designs have improved opening strength, which may facilitate removal of impacted calculi.

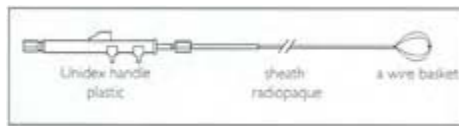


**Figure 4.19A,B** Flat-wire stone extractor. (Courtesy of Cook Urological, Spencer, Indiana.) Flat-wire baskets are nonhelical and are

designed to have larger spaces between the wires to allow engagement of larger stones.

easily engage calyceal stones. When used for ureteral calculi a flat-wire basket should be opened alongside rather than above the stone. They are also useful for the biopsy of papillary ureteral tumors.<sup>22</sup>

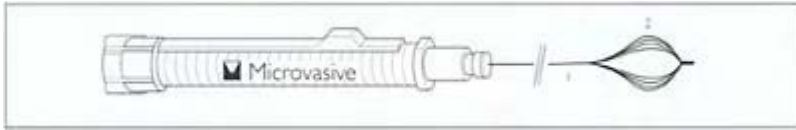
Stone basket diameters vary in size from 1.9 to 7.0F, with baskets for ureteroscopy 3.0F or less, and larger sizes for percutaneous nephrostolithotomy. A new addition is the tipless, nickel-titanium (nitinol) stone basket (Figure 4.20). The soft nitinol wires have memory, maintain their shape, resist kinking, and therefore open safely and reliably. This basket is particularly useful for percutaneous applications, but because it may permit safer disengagement of larger calculi, may also be used within the intrarenal collecting system through the flexible ureteroscope. Other basket designs such as the Parachute (Figure 4.21) (Boston Scientific, Natick, Massachusetts) and the SurCatch™ (Figure 4.22) (Circon ACMI, Stamford, Connecticut) have more wires exposed on the distal end of



**Figure 4.20** N-Circle nitinol tipless stone extractor. (Courtesy of Cook Urological, Spencer, Indiana.) A nitinol stone basket is useful in the intrarenal collecting system with a flexible ureteroscope because of its softness and its ability to disengage from a stone.

the basket, making them effective for removing multiple small fragments.

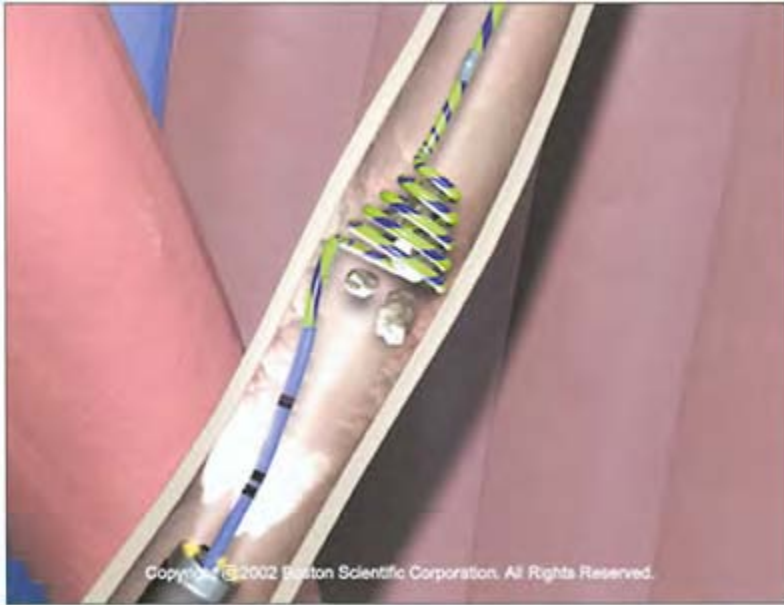
The latest development in stone retrieval devices is the Stone Cone (Figure 4.23) (Boston Scientific, Natick, Massachusetts).<sup>23</sup> This is a 3F device with a distal coil that can be deployed above the stone prior to fragmentation to help prevent stone migration. Following fragmentation of



**Figure 4.21** Microvase Leslie Parachute™ stone retrieval device. (Courtesy of Boston Scientific, Natick, Massachusetts.) The unique basket geometry allows efficient capture and retention of multiple stone fragments.



**Figure 4.22** Sur-Catch™ paired-wire basket. (Courtesy of Circon ACMI, Stamford, Connecticut.) This basket has large proximal openings to facilitate stone entry while crossed distal wires capture fragments to prevent escape.



**Figure 4.23** Microvase Stone Cone™ nitinol retrieval device. (Courtesy of Boston Scientific, Natick, Massachusetts.) The Stone Cone nitinol retrieval coil is designed to sweep multiple stone fragments.

the stone, it is withdrawn to remove fragments. Any fragments too large to remove safely will be left behind because the coil simply unravels around the stone. Further experience with this device should demonstrate its clinical usefulness.

Other devices are available for ureteroscopy use. Small 3F cup biopsy forceps can be used to biopsy sessile tumors (Figure 4.24). Electrodes are available in various shapes including pencil point, ball point, angled, and straight tips (Figure 4.25). These are used for fulguration and incision procedures such as endoureterotomy and endopyelotomy.



**Figure 4.24** Flexible biopsy cup.  
(Courtesy of Circon ACMI, Stamford,  
Connecticut.) Ureteroscopic biopsy  
forceps are used to biopsy upper tract  
lesions.

### **Additional equipment**

Fluoroscopy is a critical tool during endourologic procedures, and is needed for initial ureteral and percutaneous access, monitoring during the endoscopy, and stent and/or nephrostomy tube placement. Although tables designed for urologic endoscopy with fixed fluoroscopy units are available, mobile C-arm fluoroscopy units are preferable. C-arm fluoroscopy units allow greater mobility, improved image quality, and less radiation exposure for the surgeon because the X-ray source is below the patient rather than above. Modern C-arm fluoroscopy units incorporate digital enhancement of the image and last image-hold technology to minimize radiation exposure to the patient and surgeon. Older units without these features should not be used. Urologic endoscopy tables allow fluoroscopy of the entire abdomen, positioning of the patient in lithotomy, and should support at least 500 lb (227 kg) of patient weight. Additional features such as the ability to position the patient in the prone split-leg position for percutaneous procedures are also desirable.

### **Conclusions**

This chapter has only scratched the surface of available devices used for endourologic procedures. Detailed knowledge about instruments and their relative advantages and problems can be the difference between success and failure. Endourologists are only as good as their instruments, and appropriate choice and use of these devices can contribute greatly to improved patient outcomes.



**Figure 4.25** Flexible electrodes.  
(Courtesy of Circon ACMI, Stamford,  
Connecticut.) Different shapes of  
electrodes are available for  
fulgurations and incisions with the  
ureteroscope.

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## 5

# Laparoscopic instrumentation and equipment

Stephen V Jackman and Jay T Bishoff

The advancement of laparoscopic surgical technique goes hand in hand with the development of laparoscopic instrumentation. Only the surgeon's imagination and the willingness of industry to produce innovative equipment limit the development and application of new devices. In this chapter we describe the current state of the art in laparoscopic instrumentation with the goal of increasing surgeons' knowledge of the devices available to assist them in their laparoscopic surgical procedures. Many instruments, although not essential, are advantageous in condensing the learning curve, shortening procedure times, and improving outcomes.

### Access

A significant number of complications during laparoscopic surgery occur at the time of initial access to the peritoneal cavity.<sup>1</sup> The traditional method of Veress needle insufflation followed by blind insertion of a cutting trocar is being replaced by numerous more controlled and theoretically safer techniques. These include use of dilating-tip trocars, visual obturators, and variations on the open Hasson technique. Balloon inflation may be used to rapidly develop the retroperitoneal or retropubic spaces.

Blind-cutting trocars offer rapid access to the peritoneal cavity. Their sharp blades require less force than blunter options. However, their safety has been questioned for initial port placement, especially in the non-virgin abdomen. Even utilizing these trocars during secondary trocars placed under direct internal vision, the risk of laceration of body wall blood vessels and muscle exists. Transillumination of the abdominal wall is seldom useful for locating blood vessels, except in thin patients. Finally, cutting trocars  $\geq 10$  mm make incisions in the fascia that require closure. For these reasons, dilating-tip or non-bladed trocars were developed. Many manufacturers offer versions of this style of trocar (Figure 5.1). The tips are typically cone-shaped, often with laterally placed fins to assist in the dilation. The fins can vary from sharp to dull. Advantages include smaller fascial openings after port removal that do not require closure and a higher likelihood of pushing aside rather than lacerating blood vessels and



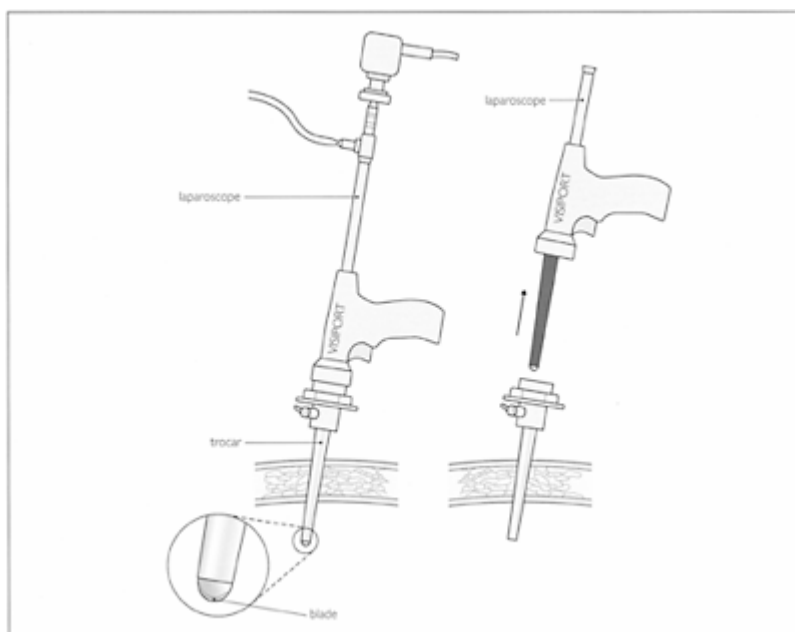


**Figure 5.1** The 10/12 mm bladeless trocar with tip close-up (Ethicon Endo-Surgery, Cincinnati, Ohio).  
(Composite of photos courtesy of Ethicon Endo-Surgery.)

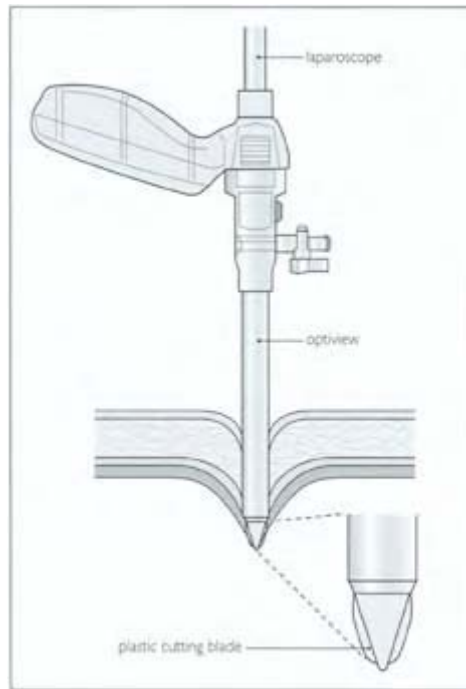
muscle.<sup>2</sup> This technology may be combined with direct visualization as described below. Disadvantages include a higher insertion force and increased difficulty penetrating compliant structures such as the peritoneum and bladder.<sup>3</sup>

Visual obturators or direct-view trocars are systems combining sheath, cutting, or dilating elements and laparoscope. These systems allow direct visualization of the layers and blood vessels of the body wall during entry. These devices are typically used after insufflation. However, with experience, they may be used for both initial access and insufflation. Two disposable instruments in this category are the Visiport RPF Optical Trocar (USSC, Norwalk, Connecticut), shown in Figure 5.2, and the Optiview Nonbladed Obturator (Ethicon Endo-Surgery, Cincinnati, Ohio), (shown in Figure 5.3). The Visiport uses a triggeractivated cutting blade to enter the abdomen, whereas the Optiview has two dilating fins. The Optiview requires more pressure and rotation to enter the abdomen but retains the advantages of non-bladed instruments, including smaller fascial defects that may not require closure. The EndoTIP system (Karl Storz GmbH & Co. KG, Tuttlingen, Germany) is a reusable threaded screw-in trocar that allows visualization and also incorporates a dilating tip.

Arguably the safest method for entrance to the peri-toneal cavity is by the open Hasson technique. Open access is particularly important in children, in whom standardized laparoscopic trocars may be more likely to damage vital structures. Disadvantages of the Hasson technique include the need for a larger incision, more cumbersome trocar systems that may leak gas if not well-secured, and increased difficulty in obese patients. The Step System (formerly InnerDyne, Inc.; now USSC, Norwalk, Connecticut) is a modification of this method that solves some of these problems (Figure 5.4). Through a small skin incision, the fascia and peritoneum are opened 2–3 mm



**Figure 5.2** The Visiport (USSC, Norwalk, Connecticut) uses a recessed blade that extends out of the end of the obturator as the surgeon fires a trigger.



**Figure 5.3** The Optiview (Ethicon Endo-Surgery, Cincinnati, Ohio) uses two sharpened plastic fins on the tip of the trocar.

under direct visualization. The mesh sleeve is then inserted and dilated with a rigid cannula and dilator to the desired size (5–12 mm). This radial dilation both fixes the sheath in place and seals the peritoneal cavity, preventing gas leakage. The access may also be conveniently upsized if needed by inserting a larger rigid sheath and dilator. The entire system can also be used over a Veress needle. However, the advantages of open insertion are lost. The fascial defect left after removing a Step trocar has been shown to be 50% smaller than that associated with a conventional cutting trocar.<sup>4</sup> Overlying tissue and muscle planes return to their preoperative location after removal and provide further closure of the wound. A prospective randomized trial in 250 patients showed that the Step system results in significantly less intraoperative cannula site bleeding and fewer postoperative wound complications than conventional cutting trocars.<sup>5</sup> Furthermore, no port-site hernias were seen despite not closing any of the Step port sites.

Another modification of the Hasson technique for access to non-peritoneal locations is use of a balloon to



**Figure 5.4** The Step System (USSC, Norwalk, Connecticut). The mesh sleeve can be placed in an open fashion or used with a Veress needle as shown. The cannula and dilator is then passed through the sleeve. (Photos courtesy of United States Surgical, a division of Tyco Healthcare.)

rapidly develop the space. This was initially done using a red-rubber catheter with a glove finger secured to the end. More convenient commercial products that perform the same task are now available. A useful combination of balloon and visual obturator, the Preperitoneal Distention Balloon System (PDB; formerly Origin Medsystems; now USSC, Norwalk, Connecticut) or Spacemaker II Balloon Dissector (formerly GSI, Inc.; now USSC, Norwalk, Connecticut) is available to allow direct observation during space creation (Figure 5.5). A balloon-tipped or Hasson trocar is required to seal the initial incision. The Blunt-tipped Trocar (USSC, Norwalk, Connecticut) is a significant advance over the standard Hasson trocar. It has a balloon at the distal end to hold it in place and a sliding foam ring proximally to seal it to the abdomen. This allows full 360° motion without leakage in a small footprint device.

### Retraction

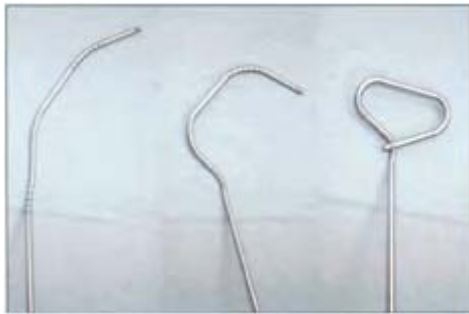
Prolonged retraction of organs such as the liver and bowel is often necessary for access to the operative site. When adequate gravity retraction is not possible, numerous



**Figure 5.5** The PDB System (USSC, Norwalk, Connecticut). The retroperitoneal space can be balloon developed under direct vision.

instruments are available. The ideal retractor would fit through a small trocar, hold the target organ securely and atraumatically, remain exactly where it was placed, and be either reusable or inexpensive. Most current instruments accomplish the first two conditions with reasonable success. They are typically variations on the design of a straight 5 or 10 mm instrument that transforms into a wider configuration once inserted.

An innovative reusable device is the Diamond Flex 80 mm Angled Triangular Liver Retractor (Genzyme Surgical Products Corp., Tucker, Georgia) (Figure 5.6). This long multi-jointed instrument passes through a 5 mm port and then transforms into a rigid triangular shape after its knob is tightened. Other sizes and configurations exist.



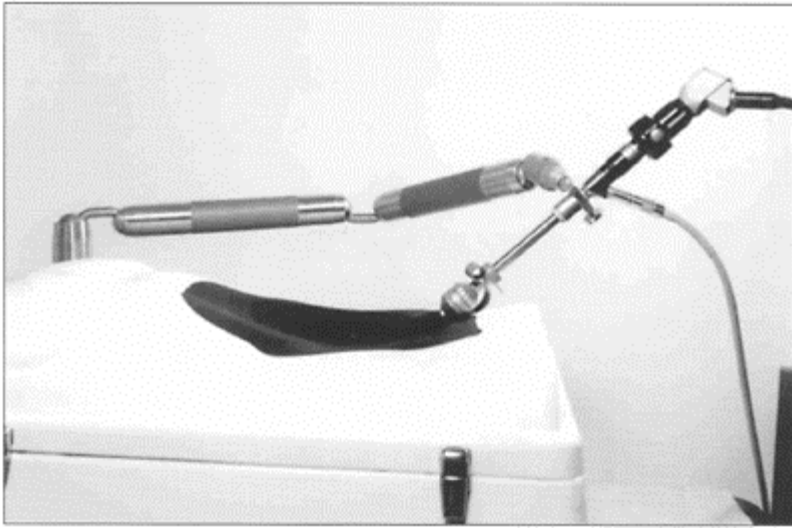
**Figure 5.6** The Diamond Flex 80 mm Angled Triangular Liver Retractor (Genzyme Surgical Products Corp., Tucker, Georgia) fits through a 5 mm cannula and converts to a rigid angled triangular shape.

Disadvantages include the initial expense and the metal construction that does not hold organs as securely as some disposable fabric devices. The PEER retractor (Jarit Surgical Instruments, Hawthorne, New York) is another reusable device that opens to provide retraction in a variety of situations. It is available in 5 and 10 mm sizes.

Fan retractors are available from several manufacturers in either a reusable or disposable form. They typically fit through a 10 mm port and 'fan' open into a triangular shape. Other common variations include balloons and fabric that expand after insertion. One significant disadvantage of the previously described instruments is that they require an assistant to reliably hold them in position. This introduces the human factors of fatigue and inattention, which can cause lack of retraction, often at the worst possible moment. In addition, the assistant takes up space at the side of the table and can hinder the optimal movement and positioning of the surgeon. Several mechanical instrument holders have been developed to take the place of the assistant. The instrument is then positioned and locked in place by one of several methods. The basic Martin Arm (Mick Radio-Nuclear Instruments, Inc., Mount Vernon, New York) is a multi-jointed stainless steel arm that requires each joint to be positioned and hand-tightened. The Unitrac Retraction System (Aesculap, Center Valley, California) is an advanced version of the Martin Arm that uses compressed air to allow pneumatic locking and unlocking with a single button (Figure 5.7). The Endoholder (Codman Inc., Cincinnati, Ohio) is an innovative device with a flexible gooseneck that can be quickly bent into position.<sup>6</sup> The TISKA Endoarm is a system developed to assist with trocar and instrument positioning (TISKA Endoarm, Karl Storz, Endoskope, Tuttlingen, Germany). This device maintains the position of the trocar sheath at a fixed point at the trocar puncture site, while instruments or laparoscopes are changed or removed. Routine laparoscopic needs such as tissue retraction can easily be performed with this system. When combined with a robotic camera holder, these instrument holders permit many procedures to be done completely without assistance.

### **Hand-assist devices**

The merits of hand-assisted laparoscopy (HAL) vs pure laparoscopy in urology are a matter of significant current debate. Proponents point to the proven ability to decrease operative times, allow performance of complex procedures, and aid in resident teaching.<sup>7</sup> This is achieved with a slight increase in postoperative pain but no significant increase in recovery times.<sup>8</sup> The issue of cost can be balanced by shorter operating room times and decreased need for other disposables such as trocars and entrapment



**Figure 5.7** The Unitrac Retraction System (Aesculap, Inc., Center Valley, California) is locked in place with compressed air. It can hold various instruments for retraction. (Photo courtesy of Aesculap, Inc.)

bags. Furthermore, injuries related to Veress needle and initial trocar access should be eliminated, as all of the HAL devices except the Pneumo Sleeve can be used for primary insufflation. The GelPort and Lap Disc also allow airtight passage of the laparoscope to visually direct subsequent port placement.

Opponents object to hand-assisted techniques because they are not actually minimally invasive since HAL requires an incision large enough to allow placement of the surgeon's hand into the abdomen. The same complex cases are being done 'purely laparoscopically' by experts, often in shorter times than those reported in hand-assisted series. These experts argue that use of the hand is a 'crutch' rather than a 'bridge' to improved surgical ability.<sup>9</sup> Other disadvantages of HAL include device failure, air leakage, hand pain and fatigue with extended dissection or tight incisions, decreased view and working room due to the intraabdominal placement of the surgeon's hand, and cosmetic concerns created by the larger incision.

Currently, there are six FDA-approved devices available for HAL surgery (Table 5.1). They all incorporate two basic features: an airtight seal between the device and the incision and a second seal between the device and the surgeon's arm (Figure 5.8). In general, devices using adhesive to seal the incision require a larger footprint and may offer more interference with choice of port-site locations. They also will not provide a reliable seal when placed so that the adhesive is near the umbilicus. An loban drape (3M Health Care, St. Paul, Minnesota) may be helpful in improving the durability of the

adhesive seal. Regardless of the device chosen, some gas leakage can be expected, especially in longer operations. A high-flow or dual insufflation system is desirable.

Little data exist comparing the different HAL devices. A recent prospective evaluation of three HAL devices (HandPort, Intromit, and Pneumo Sleeve) showed highest overall satisfaction with the Intromit.<sup>10</sup> It was easier to exchange hands or lap pads with the Intromit or HandPort than with the Pneumo Sleeve. The HandPort was the easiest to set up but also had the highest failure rate. Surgeons are encouraged to try several devices before selecting one for routine use.

**Hemostasis**

Some of the most significant advances in laparoscopic instrumentation have been achieved in hemostasis. Excessive bleeding from even small venous vessels can

**Table 5.1** *Hand-assisted laparoscopic devices*

|                  | Pneumo Sleeve  | Omniport   | HandPort                                     | GelPort   | Intromit  | Lap Disc                               |
|------------------|--|--|--|---|---|--|
| Company          | Week Closure Systems, Research Triangle Park, North Carolina | Week Closure Systems, Research Triangle Park, North Carolina | Smith & Nephew, Inc., Andover, Massachusetts | Applied Medical, Rancho Santa Margarita, California | Applied Medical, Rancho Santa Margarita, California | Ethicon Endo-Surgery, Cincinnati, Ohio |
| Seal to incision | Adhesive   | Inflation/wound retractor                                    | Inflation/wound retractor                    | Wound retractor                                     | Adhesive  | Wound retractor                        |
| Seal to arm      | Sleeve   | Inflation  | Sleeve                                       | Gel   | Inflation   | Iris                                   |
| Cost             | \$495  | \$440  | \$375  | \$725   | \$495   | \$440                                  |



**Figure 5.8** The Pneumo Sleeve (Week Closure Systems, Research Triangle Park, North Carolina) in cross section showing the airtight seals between the



device and abdominal wall and the device and the surgeon's arm. (Photo courtesy of Week Closure Systems.)

quickly obscure the surgical field, making it difficult to find the correct planes of dissection. The availability of new delivery systems for electrocautery, ultrasound, clips, staples, clamps, and fibrin products has allowed laparoscopy to approach open surgery in even the most challenging cases.

### *Electrocautery*

Monopolar electrocautery has been the mainstay for hemostasis of small vessels during dissection. In the monopolar circuit the active electrode is in the surgical site and the return electrode is the grounding pad. Consequently, the current passes through the body of the patient to complete the circuit. The waveform can be continuous or intermittent (cut or coagulation) and is low current with high voltage.

When monopolar electrocautery is used, the current is not localized to the visible portion of the instrument. Since only 15% of the entire length of the electrocautery instrument is seen with the laparoscope at any given time, injuries from stray energy can occur out of the surgeon's field of view.<sup>11</sup> More than half of laparoscopic bowel injuries reported in the literature result from monopolar electrocautery.<sup>12</sup> Application of monopolar electricity to duct-like strands of tissue attached to the bowel, even during a short burst of energy, can result in tissue death at the bowel segment.<sup>13</sup> Unrecognized bowel injuries can also occur from the use of monopolar electrocautery when stray energy is released from unrecognized breaks in the integrity of the insulated coating or from capacitive coupling along the shaft of the monopolar instruments or trocar.

The occurrence of cautery injury can be minimized through the use of active electrode monitoring (AEM) devices or insulation scanners for monopolar instruments and bipolar electrocautery. The Electroscope AEM system (Electroscope, Inc., Boulder, Colorado) includes a unique set of laparoscopic instruments that are simultaneously connected to a standard electrocautery machine and to a separate device that continuously searches for stray energy escaping along the shaft of the instrument. When stray energy is detected, the AEM system deactivates the electrosurgical generator before injury can occur. The integrity of the insulated coating on the shaft of laparoscopic instruments can also be determined on the back table, prior to placing the instrument into the patient, using the InsulScan (Medline Industries, Inc., Mundelein, Illinois). Both disposable and reusable instruments can be tested for visually undetectable holes in the insulation sheath.

In bipolar electrocautery, the active electrode and the return electrode functions are performed at the site of surgery between the tips of the instrument. The waveform is continuous, low current, and low voltage. Since the flow of current is restricted between the contact points of the instrument tip, only the tissue grasped is included in the electrical circuit, minimizing the risk of injury from stray surgical energy. Thermal injury can be prevented by vigilant surveillance of monopolar contact points during dissection.

The Ligasure is a specialized electrosurgical generator/ instrument system that has been developed (Valleylab, Boulder, Colorado) to reliably seal tissue and blood vessels up to 7 mm in diameter during laparoscopic or open surgery. The electrical generator

delivers a continuous waveform of low-voltage, high-current flow and pulsed electrosurgical energy to tissue between the jaws of the instrument. The tissue is under a predetermined amount of pressure set by the unique locking jaws of the instrument. The vessel lumen is obliterated as collagen and elastin in the vessel wall fuse to form a permanent seal. The seal zone is then divided with standard laparoscopic scissor. The newest version (Ligasure Atlas, Valleylab, Boulder, Colorado) is a 10 mm instrument that incorporates a blade in the jaws of the instrument to divide the obliterated tissue safely.

### *Argon gas coagulation*

Argon gas enhanced coagulation is useful in partial nephrectomy and in the treatment of injury to the liver and spleen. This system uses the properties of electrosurgery and a stream of argon gas to improve the delivery of the electrosurgical current. Argon gas is noncombustible and inert, making it a safe gas to use in the presence of electrosurgical current. The argon gas is ionized by the electrical current, making it more conductive than air. The highly conductive stream of argon gas provides an efficient pathway for delivering the current to tissue, resulting in hemostasis. The flow of argon gas also disperses blood, improving visualization during coagulation. During argon beam coagulation, the pressure inside the abdomen can quickly rise above the preset level. Consequently, an insufflation port should be opened during coagulation and the intra-abdominal pressure carefully monitored.

### *Ultrasound*

A relatively new tool for laparoscopic dissection uses ultrasonic energy to achieve precise cutting and coagulation. Three devices are currently available (The UltraCision System, Ethicon Endo-Surgery, Cincinnati, Ohio; The AutoSonix System, USSC, Norwalk, Connecticut; and SonoSurg, Olympus America, Inc., Melville, New York). Energy is delivered using a laparoscopic 5 mm or 10 mm handpiece with a shaft tuned to conduct the ultrasonic vibration at the rate of approximately 55,000 cycles/s. The vibration causes heat, which is more precisely located at the vibrating tip, and, at 50–100°C, is much lower than conventional electro cautery. Different tip configurations are available, including hooks, shears, and blunt probes. As the tissue is compressed between the jaws of the shears, blood vessels are occluded and the vibration causes intracellular water vaporization. Proteins are denatured in the tissue and protein coagulum forms, sealing blood vessels while tissue is divided. Hemostasis and division of tissue occur at temperatures less than conventional cautery, without the wide dispersion of heat, creating a small band of tissue necrosis. Water vapor is emitted in the abdomen instead of smoke. While the cords are reusable for all three systems, only the Olympus SonoSurg offers an autoclaveable, reusable handpiece.

### *Temporary vessel occlusion*

Laparoscopic partial nephrectomy is now possible due to instruments that allow temporary occlusion of the renal hilar vessels. Two manufacturers offer bulldog clamps

that are endoscopically applied through a 10 mm trocar. The jaws range in size from 17 to 45 mm, and come in curved and straight configurations (Klein Surgical Systems, San Antonio, Texas; Aesculap, Inc., Center Valley, Pennsylvania) (Figure 5.9). A 5 mm laparoscopic Statinsky clamp is also available but requires the placement of an additional trocar (Klein Surgical Systems, San Antonio, Texas).

#### *Surgical clips*

Occlusive clips are useful for small veins and arteries, and have become standard equipment in most laparoscopic cases. As in open surgery, clips provide a rapid alternative for hemostasis. Most endoscopic clips today are made of titanium, and vary in size from 5 to 12 mm. Non-absorbable polymer locking clips are also available and offer the advantage of being radiolucent (Week Closure



**Figure 5.9** Laparoscopic bulldog clamp and applier (Klein Surgical Systems, San Antonio, Texas).



**Figure 5.10** Hem-o-lok polymer clips (Week Closure Systems, Research Triangle Park, North Carolina). (Photo courtesy of Week Closure Systems.)

Systems, Research Triangle Park, North Carolina) (Figure 5.10). However, each clip is loaded separately on a reusable 10 mm applicator. There are absorbable clips, and some research shows no difference in adhesion formation between metallic and absorbable clips.<sup>14</sup>

Most laparoscopic clip applicators are single use and multiloop, carrying between 15 to 30 clips per unit (Table 5.2). The ability to fire multiple clips without exiting the abdomen to reload can save significant time and decrease blood loss. In general, the diameter of the shaft depends on the size of clips. The Endoclip (USSC, Norwalk, Connecticut) 5 mm shaft single-use clip applicator can deliver a slightly larger clip than other 5 mm clippers: its hinged jaws are normally retracted within the shaft, but upon squeezing the handles they advance and expand and a clip is automatically loaded. Most disposable clip applicators have 360° rotating shafts, allowing the handle of the instrument to rest comfortably in the hand while placing the tips around the target tissue at an ideal angle. Right angle clip applicators (USSC, Norwalk, Connecticut) are also available and can offer a visual advantage in situations where the tips of straight applicators are not well seen.

### *Tacking staples*

The laparoscopic biting stapler was originally developed for laparoscopic hernia repair with mesh, but these devices are also useful in refashioning the peritoneum in laparoscopic ureterolysis and fixing mesenteric defects in bowel resections. Much like the staplers used for skin wound closure, laparoscopic staplers fire titanium staples with sharp ends that enter the tissue and then undergo deformation into a rectangular shape. Most contemporary devices are single use and multi-load, with 15–30 staples/unit. A 360° rotating shaft allows accurate placement of the staple. Some devices also come with a 60–65° distal articulating head, which permits tacking hard-to-reach areas like the anterior abdominal wall and deep pelvis.

### *Linear staplers*

Laparoscopic linear staplers are essential for rapid, safe intracorporeal tissue division and reapproximation of visceral structures. With a squeeze of a handle, these devices deploy multiple, closely spaced parallel rows of titanium staples. Staples come in three different ‘loads’—thin/vascular, medium, and large/thick—and are color-coded for easy recognition. Thin staples penetrate tissue to a depth of 2–2.5 mm, deform to an exaggerated b-shape, and form a reliably hemostatic staple line. These staples are

**Table 5.2** *Clip applicators (multi-load, single use)*

|               | Ligaclip<br>Allport     | Ligaclip ERCA                  | Right Angle<br>AccuClip | Endoclip 5<br>mm | Endoclip II            |
|---------------|-------------------------|--------------------------------|-------------------------|------------------|------------------------|
| Company       | Ethicon                 | Ethicon                        | USSC                    | USSC             | USSC                   |
| Port size     | 5 mm                    | 10 and 12 mm                   | 8 mm                    | 5 mm             | 10 mm                  |
| Clips         | 20                      | 20                             | 20                      | 12               | 20                     |
| Clip<br>sizes | Medium,<br>medium/large | Medium,<br>medium/large, large | Medium/large            | Medium/large     | Medium/large,<br>large |
| Clip load     | Automatic               | Automatic                      | Automatic               | Separate lever   | Automatic              |

|   |       |       |       |       |       |
|---|-------|-------|-------|-------|-------|
| Cost  | \$288 | \$218 | \$210 | \$327 | \$236 |
| Ethicon=Ethicon Endo-Surgery, Cincinnati, Ohio; USSC=USSC, Norwalk, Connecticut |       |       |       |       |       |

ideal for rapid division of vascular pedicles. Medium-to-large staples are 3.0–4.8 mm thick in their closed form, and are useful in securing thicker tissues like bowel, bladder, and ureter. The larger staples do not fold to the same tight shape as small staples and should not be used for primarily hemostatic ligation. Staplers today allow the same instrument to fire between 8 and 25 separate loads before stapler disposal.

Linear staplers can be broadly classified into cutting and non-cutting. Cutting versions deploy loads with six intercalated parallel rows of staples. As the staples are fired, a knife follows closely behind and incises the tissue between the staples, leaving three rows of staples on each side. The staple line extends past the range of the cutting knife by one or two staples to avoid incising non-secured tissue. Once the staples are fired, a safety feature on all devices prevents accidental re-deployment of the cutting knife until a new load with staples is in place. Non-cutting staplers simply fire three to four parallel rows of staples, and are useful for closing enterotomies and repairing bladder injuries.

Laparoscopic linear cutting staplers are further distinguished by the length of their staple line (30/35, 45, and 60 mm), and whether their firing heads are articulated or not (Table 5.3). An articulating head gives a greater range of motion from a fixed trocar but also adds to the price. All devices offer a rotating shaft, which allows proper visualization of the tips during firing. On most models, a replacement load consists of a fresh six rows of staples but uses the same knife and anvil inherent to the actual stapling device. The Endo GIA Universal linear cutting stapler is a universal firing device that accommodates both articulating and non-articulating loads of varying lengths (30, 45, and 60 mm) (USSC, Norwalk, Connecticut). The stapler is unique in that the jaws, anvil, and knife are inherent to the load and not part of the actual base unit; i.e. each re-load comes with a new knife. Also, this system allows the surgeon to use loads (articulating or fixed) of varying lengths without having to open a new stapler. The minimum-size limitation posed by the width of the staple load requires use of a 10 mm or larger port for all currently available staplers.<sup>15</sup>

### *Loop ligation*

Loop ligatures are valuable in securing an already transected pedicle. A length of suture with a pre-formed sliding, locking knot is passed intracorporeally. The structure to be ligated is then retracted through the loop with a grasper, and the loop cinched down with a knot pusher. Two loop ligation systems are available with both 0 and 2–0 plain gut, chromic gut, polyester, and synthetic absorbable varieties (Surgitac, USSC, Norwalk, Connecticut; Endoloop, Ethicon, Cincinnati, Ohio). The plastic knot pusher is only available in one length, and may be too short to reach the target site if the wrong port is chosen. Two hands are needed to cinch the knot, requiring an assistant to grasp the tissue and hold it still.

*Fibrin products*

Fibrin tissue adhesive (FTA) has gained widespread acceptance in a variety of surgical procedures as an adhesive,

**Table 5.3** *Linear staplers*

|                   | Endopath<br>ETS         | Endopath<br>ETS/flex<br>articulating | Endopath<br>EZ45:<br>cutter | Multifire<br>Endo<br>GIA 30 | Multifire<br>Endo<br>TA | Endo<br>GIA<br>Universal     |
|-------------------|-------------------------|--------------------------------------|-----------------------------|-----------------------------|-------------------------|------------------------------|
| Company           | Ethicon                 | Ethicon                              | Ethicon                     | USSC                        | USSC                    | USSC                         |
| Port size         | 12 mm                   | 12 mm                                | 18 mm                       | 12 mm                       | 12 mm                   | 12 and 15 mm                 |
| Staple size       | 2.5, 3.3, and<br>4.1 mm | 2.5, 3.5, and<br>4.1 mm              | 3.8 and 4.5<br>mm           | 2.0, 2.5, and<br>3.5 mm     | 2.5 and 3.5<br>mm       | 2.0, 2.5, 3.5,<br>and 4.8 mm |
| Staple<br>length  | 35 and 45<br>mm         | 35 and 45 mm                         | 45 mm                       | 30 mm                       | 30 mm                   | 30, 45, and 60<br>mm         |
| Rotating<br>shaft | Yes                     | Yes                                  | Yes                         | Yes                         | Yes                     | Yes                          |
| Articulating      | No                      | Yes                                  | No                          | No                          | No                      | Yes                          |
| Cost              | \$399                   | \$498                                | \$495                       | \$433–500                   | \$433–500               | \$433–500                    |

Ethicon=Ethicon Endo-Surgery, Cincinnati, Ohio; USSC=USSC, Norwalk, Connecticut.

sealant, hemostatic agent, or carrier for growth factors or antibiotics. Fibrin products have been used in many different urologic procedures to assist with hemostasis and tissue adhesion.<sup>16,17</sup> FTA can also be valuable in treating complications of laparoscopic surgery, including spleen and liver injury, urinary fistula formation, and wound dehiscence.<sup>18</sup> Presently, FTA is made from autologous preparations using a patient's own blood or from homologous sources using a single donor or pooled samples.

Concentrates of coagulation factors are known for their adhesive and coagulation properties. In addition, fibrin in surgical wounds promotes healing by supplying a network for the growth of fibroblasts and activating macrophages.<sup>19</sup> Surgeons have prepared their own fibrin sealants for many years. However, these locally prepared products are not standardized and the sources of fibrinogen are not virally inactivated. Commercially available blood-derived products are now available for topical application to control bleeding and seal tissue. The basic principle is the same for these kits. Human thrombin and fibrinogen are applied separately to a bleeding site, resulting in formation of a layer of fibrin that controls the bleeding and seals tissue. Eventually, the fibrin film is reabsorbed.

Commercial preparations reproduce the final stage of coagulation, resulting in their adhesive, hemostatic, and healing effects through the polymerization of fibrin chains with collagen of adjacent or damaged tissue. These fibrin sealants are made from different combinations of fibrinogen and thrombin derived from human plasma and fibrinolysis inhibitor, a substance of bovine origin. As part of normal coagulation, fibrinogen undergoes proteolysis by the enzyme thrombin to form a fibrin monomer that polymerizes into fibrin strands, making up a major component of the actual clot. Thrombin also activates clotting factor XIII, promoting cross-linking of the fibrin monomer to stabilize the fibrin network. Thrombin is found in the plasma as an inactive precursor—prothrombin. After proteolysis, the active enzyme thrombin is formed.

Proteolysis occurs as a result of tissue damage to cell membranes (extrinsic pathway) or trauma to the blood vessel walls, exposing collagen (intrinsic pathway), which results in the activation of thrombin followed by fibrin clot formation. The clotting time of fibrin sealant is dependent on the concentration of thrombin in the sealant.

Commercial fibrin sealants are typically packaged as freeze-dried concentrates of human fibrinogen and thrombin in separate containers. The powders are reconstituted and bovine fibrinolysis inhibitor (aprotinin) is added to the liquid fibrinogen. When the fibrinogen and thrombin solutions are mixed, they become active, forming a clot of adhesive (Haemacure Corp., Sarasota, Florida; Tisseel, Baxter Healthcare Corporation, Glendale, California). Another product currently available uses the patient's own plasma mixed with bovine thrombin and bovine collagen (CoStasis, US Surgical, Norwalk, Connecticut) but is FDA approved for hemostasis alone and not for tissue sealing or tissue adhesion. The American Red Cross has developed a lyophilized fibrinogen and thrombin product that is combined on a prepackaged absorbable backing (similar to a 4×4 sponge) or a powder spray. The 4×4 bandage is designed to be applied directly to the wound in open cases, while the powder formulation is readily delivered laparoscopically.<sup>20–23</sup> When these products contact the surgical site or blood, they are activated and rapidly form a dense synthetic clot. The lyophilized formulation is currently under investigation and not FDA approved for human use.

Since fibrin sealants commonly consist of human and bovine products, there is a theoretical risk of viral transmission, anaphylaxis, and coagulopathy. Viral transmission is of great concern since pooled human plasma is used to make the sealant. Donor screening, heat treatment of tissue, and solvent/detergent treatment seem to be effective in maintaining the safety of these products by preventing the transmission of HIV, Epstein-Barr virus, cytomegalovirus, and hepatitis.<sup>24</sup> However, four patients are known to have been infected with parvovirus B19 following treatment with fibrin sealant.<sup>25,26</sup> Infection with parvovirus B19 is usually asymptomatic or may present with a minor febrile illness. Rarely, transient aplastic crisis with rapid red blood cell turnover can occur. There is an isolated report of a patient who developed rash, bronchospasm, and circulatory collapse following use of fibrin sealant to close an enterocutaneous fistula. A complete investigation showed her to have aprotinin-specific anti-bodies, which were the most likely cause of the severe anaphylactic reaction.<sup>27</sup> Fibrin sealants are designed for topical use and are not designed for systemic injection. Intravenous injection could result in systemic activation of the coagulation cascade and fatal thrombosis. No systemic effects have been reported using sealants on surgical bleeding sites.

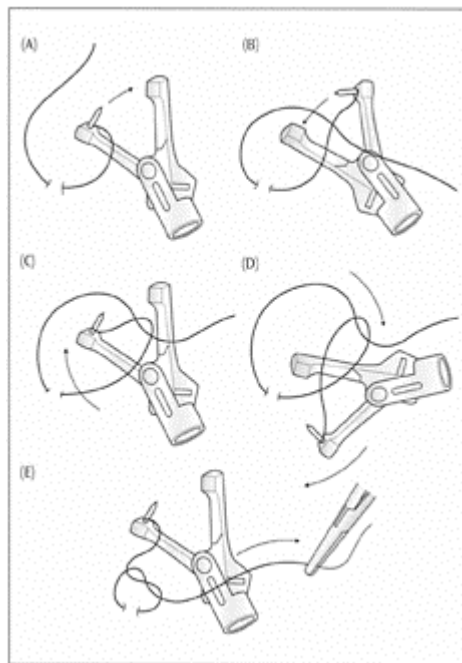
### **Suture assist**

Given the complexity of suturing in the laparoscopic environment, the majority of early laparoscopic urologic cases were extirpative and required little to no reconstruction. Unique demands to be overcome include a fixed center of motion, limited needle and suture handling ability, lack of three-dimensional perspective, and intracorporeal knot tying. Today, with the increasing interest in laparoscopic radical prostatectomy, more urologists are becoming proficient in free-hand suturing. This technique is applicable to most situations and offers the greatest flexibility with respect to suture and needle choices

as well as the angle at which a needle may be held. For special circumstances and for those less experienced in free-hand techniques, several instruments have been developed to facilitate laparoscopic suturing.

The EndoStitch (USSC, Norwalk, Connecticut) is an innovative device that passes a small needle back and forth between jaws, allowing both running and interrupted suturing techniques without the need to worry about reloading the needle. It also facilitates rapid intracorporeal knot tying (Figure 5.11). Limitations of the EndoStitch include its 10 mm width and short dull needle that cannot be passed through thick tissue and is more traumatic than a similar-sized swedged-on suture. The needle can only be passed perpendicularly from jaw to jaw and may require excess tissue manipulation for proper suture placement. Finally, the device is disposable and reloads are costly, adding to the expense of a case. Despite these disadvantages, the EndoStitch has been used very successfully, even in cases requiring delicate reconstruction such as laparoscopic pyeloplasty.<sup>28</sup>

The Suture Assist (Ethicon Endo-Surgery, Cincinnati, Ohio) is a 5 mm instrument designed to place a pretied knot quickly after using either the device or a needle driver to place a single or figure-of-eight throw. Running sutures



**Figure 5.11** Knot tying with the EndoStitch (USSC, Norwalk, Connecticut).



are not possible without using an alternative knot-tying method for the second knot. Like the EndoStitch, the Suture Assist is disposable and relies on reloads.

A newer 5 mm instrument, the Sew-Right SR5 (LSI Solutions, Rochester, New York), uses two built-in needles to place a simple suture precisely through even relatively thick tissue. Advantages include its 5 mm size and needle passage parallel to the device, which may be better for some applications. With tenacious tissue, if the needle deviates or does not fully penetrate the tissue, it may miss or not engage the suture at the distal jaw. Again, this is a disposable instrument and only a single simple suture may be placed per load.

A final device, the Quik-Stitch (Pare Surgical, Englewood, Colorado) is available in 3, 5, 10, and 12 mm versions. This system consists of a proprietary needle driver passed through a spool containing a pretied knot. A single or figure-of-eight suture is placed or passed, followed by release, setting, and advancement of the knot. The device and needle driver are reusable, making it economical. Straight, curved, and blunt needles are available on absorbable and nonabsorbable sutures.

Intracorporeal knot tying, especially the second knot of a running suture, can be complicated. This is due to the short suture length often available for tying, the need to tie a single strand to a loop, and difficulty in maintaining constant tension on a knot. Two instruments are available to assist with this task. The Lapra-Ty (Ethicon Endo-Surgery, Cincinnati, Ohio) places a resorbable polyglycolic acid clip on the tail or tails of a suture to secure a running or simple suture. This allows precise tensioning of the suture with another instrument during 'tying'. The instrument is reusable and clips come six to a pack, making it economical. A concern is that a large number of clips may incite an inflammatory reaction or fistula. It is therefore most valuable for the final 'knot' of running sutures.

A second 'knot-tying' instrument is the Ti-Knot TK5 (LSI Solutions, Rochester, New York). This device is designed to replace extracorporeal knot tying. Once the two suture ends have been brought out through the trocar, they are snared and fed through a titanium cylinder at the end of the device. While holding the sutures under the proper tension, the instrument is advanced to the closure site and fired. This crimps the titanium knot onto the suture and trims the extra. Advantages promoted by the manufacturer include precise tensioning, one-step suture tying and cutting, and titanium's nonreactivity. Disadvantages are the need for extracorporeal loading of the suture into the device and the costs of a disposable instrument.

With experience, surgeons will find most suturing and knot tying is best done with a simple needle driver and curved graspers. However, the above instruments may be useful early in one's experience and in special circumstances.

### **Tissue retrieval**

Anyone who has struggled to place an organ or tissue in a bag can immediately appreciate new advances in retrieval technology. The Endocatch (USSC, Norwalk, Connecticut) is a self-opening bag, which comes in several sizes, including 10 mm and 15 mm. Once the instrument is placed through a trocar or directly through the skin, the inner core handle slides forward, advancing the bag. A metal band automatically opens

the bag and can be used to scoop up the tissue to be removed. A separate string is pulled, closing the bag and tearing it away from the metal ring. The ring is pulled back into the handle and the device removed, leaving the closed bag and string in the working space. The current bags are not strong enough to withstand automated tissue morcellation, but are useful when intact removal of specimens is required.

If the specimen is to be morcellated, a LapSac (Cook Urological, Inc., Spencer, Indiana) fabricated from a double layer of plastic and nondistendable nylon must be used. This device has been shown to withstand morcellation and remain impermeable to bacteria and tumor cells.<sup>29</sup> In the past, placing large specimens in the LapSac was often a consuming and frustrating experience. Using several simple tricks the bag can now be modified to allow rapid entrapment of specimens. A stiff hydrophilic wire can be double passed through the holes in the LapSac, creating a rigid opening. The bag and wire can be rolled up and inserted through an 11 mm trocar site with the trocar removed. Replacing the trocar alongside the protruding ends of the wire allows the pneumoperitoneum to be reestablished. The modified LapSac opens easily and the rigid wire maintains the mouth of the sac open. Once the specimen is entrapped, the wire can be pulled from the holes in the sac and the mouth of the sac brought out through a trocar site.

### **Morcellation**

At the conclusion of any extirpative laparoscopic procedure, the organ must be removed from the patient. When malignancy is not involved and an incision is otherwise not required, morcellation and removal through the largest port site is ideal. This requires entrapment in a suitably sized pouch and mechanical reduction in size to allow passage through the port site. Morcellation of malignant lesions continues to be controversial.<sup>30,31</sup> There is clear cosmetic benefit and possibly a small decrease in postoperative morbidity with morcellation. Computed tomography (CT) has been proven to be an effective tool for planning surgery and predicting pathologic findings.<sup>32</sup> To date, there have been no reports of peritoneal seeding or local tumor recurrence in the renal fossa following laparoscopic nephrectomy with specimen morcellation. There have been two reports of trocar site seeding after radical nephrectomy. In one of the two patients it is likely that he had metastatic ascites at the time of nephrectomy.<sup>33–34</sup> No study to date has directly compared morbidity between use of morcellation vs use of an incision for specimen removal. One study compared pain and hospital stay in patients after morcellation vs those requiring conversion to an open procedure by subcostal incision.<sup>35</sup> Not surprisingly, there was less narcotic analgesic use and a shorter stay in the morcellation group. A more equal comparison would be that of HAL nephrectomy vs laparoscopic nephrectomy with morcellation. This has not shown a morbidity advantage for morcellation.<sup>8</sup> On the other hand, there has been only one reported port-site recurrence.<sup>36</sup> This was not clearly related to a morcellation accident but occurred at the appropriate port site. Finally, pathologic staging is rarely needed for treatment decisions after nephrectomy for renal cell carcinoma given excellent CT staging and the lack of effective adjuvant treatment options. This is not the case for transitional cell carcinoma, where morcellation is not recommended. In either case, prognostic information is lost with morcellation.

Once the decision has been made to morcellate an organ, it must first be placed in an impermeable bag (LapSac, Cook Urological, Inc., Spencer, Indiana). Once closed, the strings of the bag are removed through the chosen port site, removing the trocar at the same time. The area is then carefully draped with towels to prevent tumor contamination. The simplest, cheapest, and quickest option is to extend the fascial incision to 20 mm to allow manual fragmentation and extraction of the tissue using a combination of ring forceps, Kocher clamps, etc. The laparoscope should be used throughout this process to visually confirm bag integrity from inside the abdomen. The advantage of this technique is that it creates relatively large pieces of tissue and with the addition of India ink may allow preservation of much staging and margin information.<sup>37</sup>

Several instruments have been developed in an attempt to assist in the morcellation process, specifically to eliminate the need for port-site enlargement. Each is a combination of a rotating cylindrical blade with a mechanism for drawing the tissue into the device (Table 5.4). None is ideal and only one ex-vivo comparison trial exists, which attempts to quantitate morcellation time, bag integrity, and mean specimen weight.<sup>38</sup> Three morcellators were tested on human-sized kidneys without any perirenal tissue. This showed that the standard high-speed electrical laparoscopic (HSEL) morcellator (Cook Urological, Inc., Spencer, Indiana) performed the task acceptably in approximately 15 min. It was also the most economical. The Steiner morcellator (Karl Storz, Culver City, California) was twice as fast and provided specimen fragments 5 times larger (about 3 g), which may be more useful for pathologic evaluation. The Gynecare X-Tract (Ethicon

**Table 5.4** *Comparison of laparoscopic tissue morcellators*

|           | HSEL  | Steiner<br>electromechanical           | Gynecare X-<br>Tract                       | RIWO CUT  |
|-----------|---|--|--|---|
| Company   | Cook Urological,<br>Inc., Spencer,<br>Indiana | Karl Storz, Culver City,<br>California | Ethicon Inc.,<br>Somerville, New<br>Jersey | Richard Wolf Medical<br>Instrument Corp.,<br>Vernon Hills, Illinois |
| Mechanism | Suction                                       | Forceps                                | Forceps                                    | Forceps   |
| Blade     | Recessed                                      | Protrudes ~2 mm                        | Recessed with<br>manual blade<br>guard     | Reusable bare blade, no<br>sheath                                   |

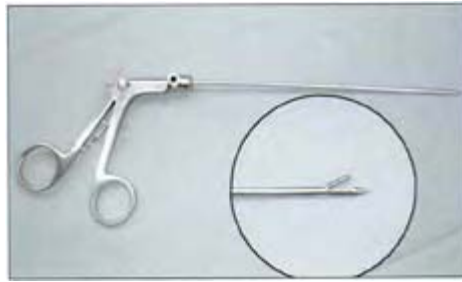
Inc., Somerville, New Jersey) and RIWO CUT (Richard Wolf Medical Instrument Corp., Vernon Hills, Illinois) devices are likely to perform similarly, given their modes of action. The modified electrical prostate morcellator (Coherent, Sturbridge, Massachusetts) was slow and expensive. A recommendation was additionally made that the use of a shortened trocar may provide increased safety by protecting the bag neck from heat and mechanical stress.

In conclusion, if the choice is made to morcellate a specimen, no current device offers a large advantage over the manual method. The Cook morcellator is currently unavailable. Use of one of the other morcellators may be time- and cost-efficient in high-volume programs and when already available in the operating room, usually as part of the gynecology instrumentation.

## Closure

Exiting the abdomen consists of visually controlled port removal and purging the carbon dioxide gas. Port sites 10 mm in size or larger have traditionally been closed to prevent port-site hernias. These have been reported to happen in up to 3% of cases.<sup>39</sup> Despite newer-style trocars that may not require fascial closure up to 12 mm, most surgeons continue to close ports  $\geq 10$  mm in adults and 5 mm sites in children.

Conventional open suture closure of port sites can be difficult, especially in obese patients. Multiple instruments have been developed to simplify and expedite this task. Most follow the same basic principle of suture passage through the fascia and into the peritoneal cavity under direct vision followed by suture retrieval with a second pass through the opposite side of the fascia. The Carter-Thomason needle-point suture passer (Inlet Medical Inc., Eden Prairie, Minnesota) and Berci fascial closure device (Karl Storz GmbH & Co. KG, Tuttlingen, Germany) are two commonly used nondisposable instruments based on this model (Figure 5.12). Both have a sharp beak which punctures the fascia and then opens to



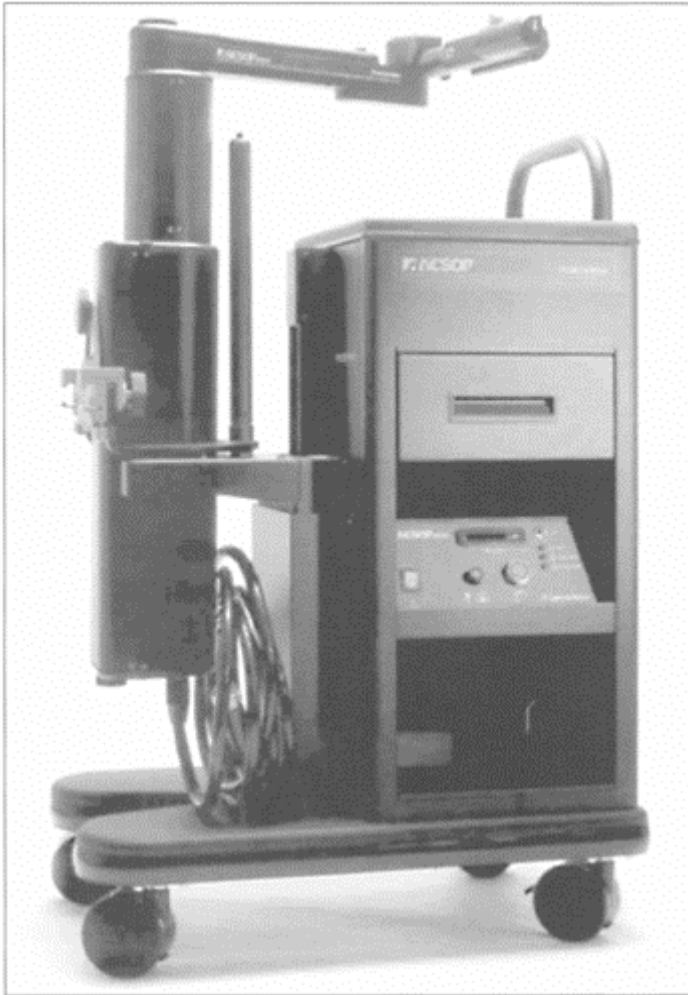
**Figure 5.12** Berci fascial closure device (Karl Storz GmbH & Co. KG, Tuttlingen, Germany) with tip close-up.

capture or release the suture. The EndoClose (USSC, Norwalk, Connecticut) is a similar disposable device. Its rigidity is less and suture capture opening smaller, making it somewhat more difficult to use.

## Robotic-assisted surgery

Once a mere fantasy, robotic-assisted surgery is now reality. Currently available robots vary in complexity and degree of involvement in the procedure. Simple robots are used for laparoscope holding and direction, while others are more directly involved in tissue manipulation at the surgeon's direction. The automated endoscopic system for optimal positioning or AESOP robotic device (Computer Motion, Inc., Santa Barbara, California) was the first FDAcleared surgical robot. The AESOP system attaches to the side of the

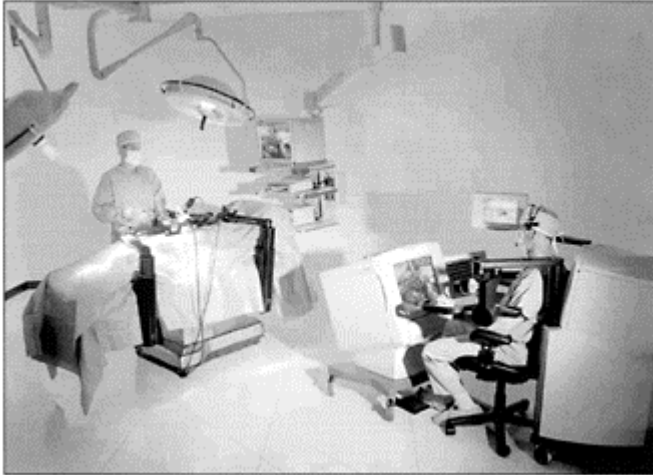
operating room table and incorporates a 7-degree of freedom robotic arm to hold and position the endoscope during laparoscopic surgery. The robot is voice-activated, allowing control by the operating surgeon, eliminating unintentional movement, and ensuring a stable surgical image (Figure 5.13).



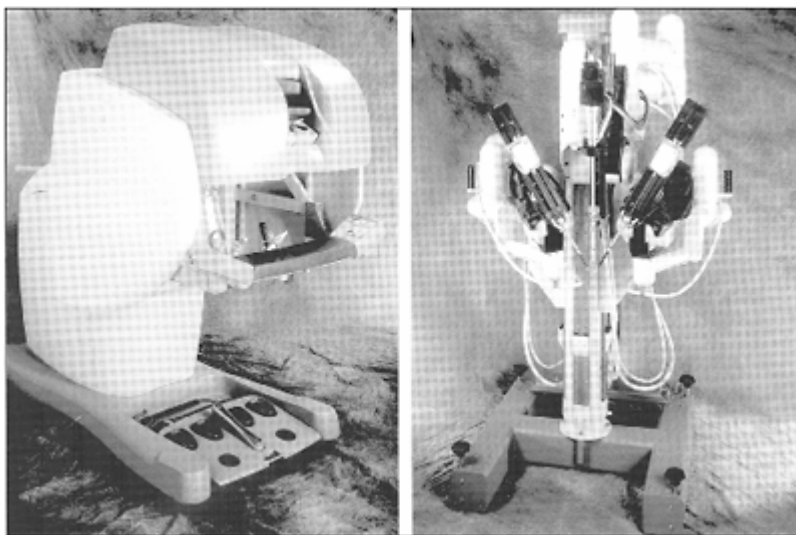
**Figure 5.13** The AESOP robot (Computer Motion, Inc., Santa Barbara, California). (Photo courtesy of Computer Motion, Inc.)

Currently two robotic systems are FDA-cleared for tissue manipulation during laparoscopic surgery. Since the surgeon actually performs the procedure with the

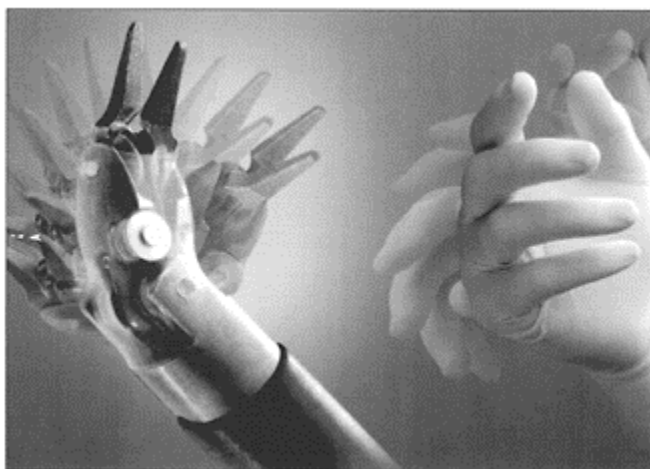
assistance of the mechanical device, these systems are not purely robotic. The ZEUS robotic surgical system (Computer Motion, Inc., Santa Barbara, California) consists of a surgeon's control console and three table-mounted robotic arms (Figure 5.14). Two arms are used for instrument manipulation and one for control of the endoscope. The da Vinci Surgical System (Intuitive Surgical, Inc., Mountain View, California) is a master-slave system that uses robotic technology with 3-dimensional visualization (Figure 5.15). The surgeon operates while seated at a console, viewing the surgical field. At the



**Figure 5.14** The ZEUS robotic surgical system (Computer Motion, Inc., Santa Barbara, California). (Photo courtesy of Computer Motion, Inc.)



**Figure 5.15** The da Vinci Surgical System (Intuitive Surgical, Inc., Mountain View, California) consists of the surgeon console and the patient side cart that provides the two robotic arms and one endoscope arm. (Photos courtesy of Intuitive Surgical, Inc.)



**Figure 5.16** The 7 degrees of freedom Endowrist (Intuitive Surgical, Inc.,

Mountain View, California) end-effector of the da Vinci Surgical System. (Photo courtesy of Intuitive Surgical, Inc.)

patient's side, three robot arms position and maneuver the Endowrist endoscopic instruments and laparoscope with a wide range of movements and 360° maneuverability through laparoscopic trocars. The instruments are capable of delivering 7 degrees of freedom, like the human wrist (Figure 5.16). The surgeon's movements are translated into movements of the instruments, allowing precise dissection, manipulation, and suturing. The da Vinci Surgical System has received FDA market clearance for use in performing many different laparoscopic procedures. In the field of urology, it has received FDA clearance for use in radical prostatectomy, and several different studies have shown the feasibility of its use in this procedure.<sup>40-42</sup>

Robotic assistance has the potential to enhance the surgeon's capabilities. The machine translates the surgeon's movements into more steady and precise results at the end of laparoscopic instruments. With these new devices there is potential to decrease the learning curve associated with traditional laparoscopic surgery where instrument movements and degrees of freedom are limited. Motion scaling allows for more precise movements from the surgeon's hand. Intention and resting hand tremor are considerably diminished compared with open surgery, but are virtually eliminated with robotics.

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## 6

# Imaging in minimally invasive urologic surgery\*

Thomas M Seay and Thomas M Dykes

Urology is only second to orthopedics as a specialty that has made extensive use of imaging in diagnosis and operative planning. Because of this reliance on imaging, rare is the situation where the urologic surgeon enters into an operation with exploration being the initial indication. Urologists, as part of their training, develop an intimate knowledge of those imaging techniques that have become essentials of their diagnostic armamentarium. Indeed, in the United States, part of the Board certification process in urology requires adeptness at specific image interpretation. That said, as surgical techniques have progressed in the last decade, so too has imaging technology. Beyond the intravenous pyelography/excretory urography (IVP/EXU), retrograde pyelogram, and cystogram, urologists of the 21st century require knowledge of ultrasound (US), newgeneration computed tomography (CT), and magnetic resonance imaging (MRI) to such a degree as never before.

The purpose of this chapter is to briefly discuss those imaging techniques which are specifically of interest to the laparoscopic urologic surgeon. Briefly discussed will be current imaging evaluation of hematuria, specifically as regards renal cell carcinoma (RCCa), adrenal lesions, preoperative imaging evaluation of ureteropelvic junction obstruction (UPJO) in adults, and preoperative imaging evaluation of patients being considered as renal donors. The chapter is by no means all inclusive, but is meant as a practical review of what issues and studies are encountered on a day-to-day basis.

\* The opinions expressed herein are those of the authors and are not to be construed as those of the United States Air Force or the Department of Defense of the United States of America.

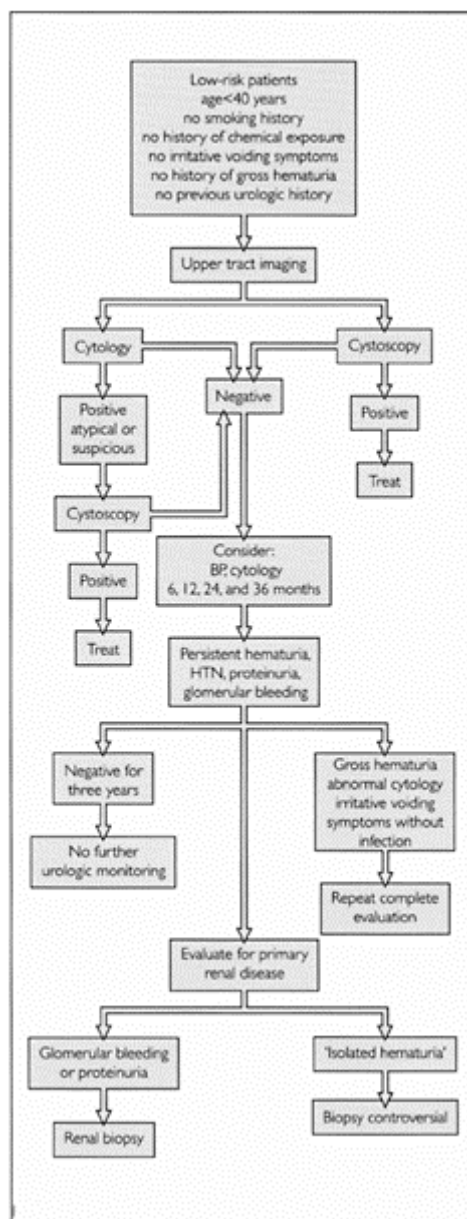
## Hematuria

The major urologic problems for which the patient seeks evaluation are hematuria, either gross—causing distress in the patient—or microscopic—causing concern in the referring provider—and obstruction. The majority of clinicians mandate work-up for gross hematuria, with the indications for work-up of microhematuria a matter of debate, usually centering on a discussion as to what ‘significant’ microhematuria is to be defined as. The definition of ‘significant’, cognizant that up to 18% of individuals have some degree of hematuria, is usually based upon the number of red blood cells (RBCs) in centrifuged urinary sediment per high-power field (HPF). The upper limit of normal is quoted as 2–3 RBCs/HPF; this cutoff has also been raised to up to 5 RBCs/HPF and also lowered to considering the presence of any RBCs at all as an indication for evaluation.<sup>1</sup> Nonetheless, the three *major* entities of concern, which asymptomatic microscopic hematuria may be a harbinger of, are RCCa, transitional cell carcinoma, and urinary stone disease. While imaging may suggest transitional cell carcinoma in a particular patient, it is an endoscopically obtained diagnosis, whereas the clinician is on firmer ground with imaging studies demonstrating a urinary calcification or a solid renal mass.

Grossfeld et al have stratified patients based upon ‘high-risk’ vs ‘low-risk’ criteria (Table 6.1) and have consequently

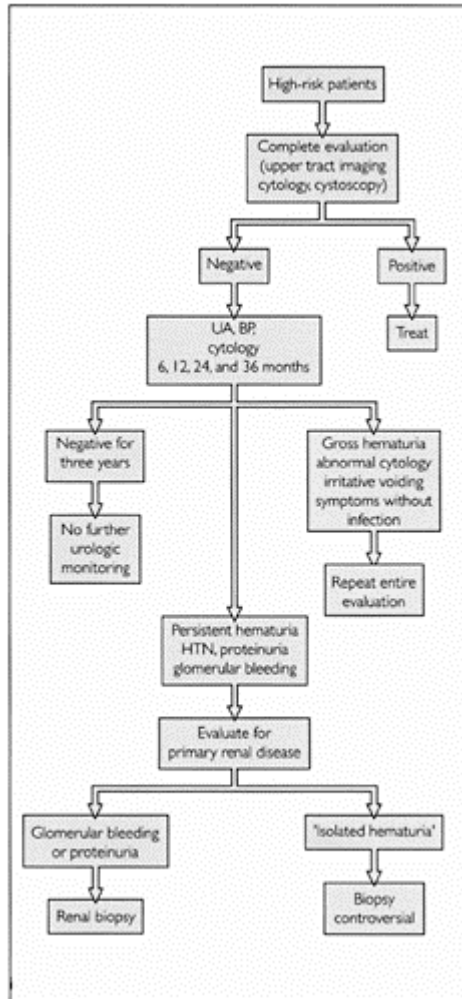
**Table 6.1** *Risk factors for disease in patients with microscopic hematuria: the ‘high-risk’ patient*

|  |
|--|
| Smoking history  |
| Occupational exposure to chemicals or dyes (benzenes or aromatic amines) |
| History of gross hematuria   |
| Age >40 years  |
| Previous urologic history  |
| History of irritative voiding symptoms                                   |
| History of urinary tract infection                                       |
| Analgesic abuse (e.g. phenacetin)  |
| History of pelvic irradiation  |
| Cyclophosphamide exposure  |
| Reproduced with permission from Grossfeld et al. <sup>2</sup>            |



**Figure 6.1** Suggested regimen for low-risk patients with asymptomatic microhematuria. Reproduced with permission from Grossfeld et al.<sup>2</sup>

proposed algorithms for evaluation based upon this stratification (Figures 6.1 and 6.2).<sup>1,2</sup> Prudence, based upon the history of the patient, is in order. Patients with microscopic hematuria that can be surmised to be due to some activity or a urinary tract infection can be reassessed with urinalysis after cessation of that activity or resolution/treatment of the presenting clinical syndrome. A period of follow-up (at 6, 12, 24, and 36 months) is also recommended as

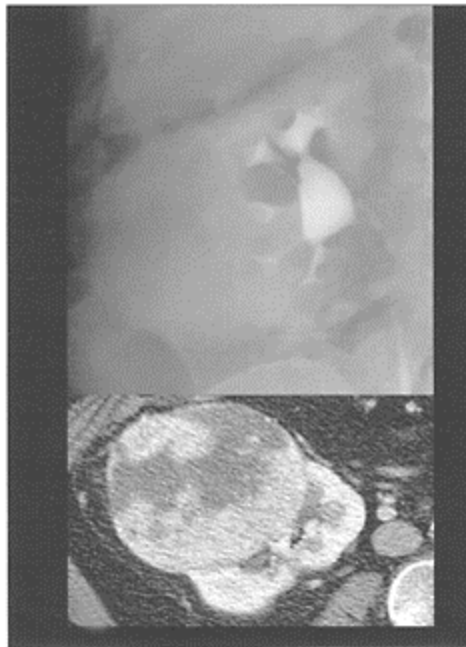


**Figure 6.2** Suggested regimen for ‘high-risk’ patients with asymptomatic microhematuria. Reproduced with permission from Grossfeld et al.<sup>2</sup>

microscopic hematuria due to a significant cause may be intermittent.

Taking the algorithms above at face value, there does not seem to be discrimination between the initial work-up between the two groups. Upper tract imaging does play a paramount role in both populations. Upper tract imaging may be performed using IVP/EXU, CT, or CT urography.

IVP is widely available, and has served for decades as the standard initial imaging modality in the work-up of hematuria. However, if one is to treat in a minimally invasive manner, one hopes to discover the disease at a stage when such treatment is still feasible and effective. As regards renal cell carcinoma, IVP, while identifying patients with larger tumors (>3 cm), is found wanting in the detection of those lesions that are best served by laparoscopy or open partial nephrectomy (Figures 6.3, 6.4, and 6.5). CT is becoming more available, and in combination with a



**Figure 6.3** Selected image from IVP-correlated CT image with contrast from same patient demonstrates large right renal mass that is readily observable on IVP.

limited IVP—which can be performed in any facility where the two modalities are physically in close proximity—complete assessment of both parenchymal and urothelial disease, as well as local staging, can be immediately obtained. The patient that is so

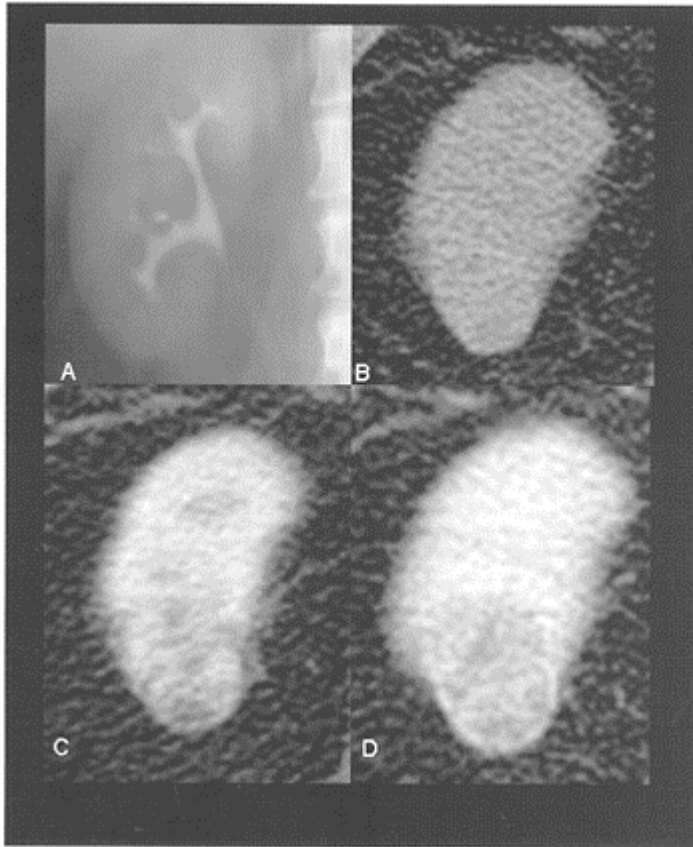
evaluated has no need to return for a CT or US when an isolated IVP detects a contour abnormality.

### **Optimal evaluation of the renal mass: intravenous pyelography, computed tomography—intravenous pyelography**

Survival from RCCa is intimately related to presenting stage.<sup>3,4</sup> This is indirectly a function of the size of the primary tumor. Limiting discussion to a T1 lesion (which under the 1997 TNM (tumor-node-metastasis) classification includes organ-confined tumors up to 7 cm in size),<sup>5</sup> further stratification has suggested a significant breakpoint in prognosis between those patients with tumors less than 4.5 cm in size and those between 4.5 and 7 cm.<sup>6</sup> Additionally, DNA content, ploidy versus nonploidy, correlates with tumor size, with one series demonstrating that 100% of tumors <3 cm, 88% of tumors >3 and <5 cm, and 28% of tumors >5 cm being diploid.<sup>7</sup> A patient with a diploid tumor less than 3 cm had a 4% risk of progression vs 43% for a diploid 10 cm tumor. Tumor size and DNA ploidy were independent factors of progression in this series, with size contributing the greater relative risk (9.32 vs 1.45, respectively) to progression. Based upon the above, it would seem that the ideal situation would be detection of the lesion when it is 3 cm or less in size.

Using CT as a reference standard, intravenous pyelography with plane tomography has been shown to be able to detect 85% of parenchymal lesions  $\geq 3$  cm, with a decline to 52% for those lesions  $\geq 2$  but <3 cm, to 21% for those lesions  $\geq 1$  but <2 cm and 10% for those lesions less than 1 cm.<sup>8</sup> Comparative numbers using ultrasound were 85%, 82%, 60% and 26%, respectively (Figure 6.6). An earlier retrospective study of patients with a solitary lesion less than 3 cm found that initial screening urography failed to identify the lesion in 66% of cases.<sup>9</sup> While these data were generated in the late 1980s, one has to remember that the basic means of performing and interpreting an IVP have not changed. Additionally, IVP, though standardized at most facilities, is subject to great variability in quality due to patient variation in preparation and habitus. Finally, while a substantial cortical lesion along the lateral surface of the kidney may be amenable to detection, lesions that are arising from the anterior or posterior surface of the kidney, or near the hilum without any discernible effacement of the collecting system, may easily escape notice.



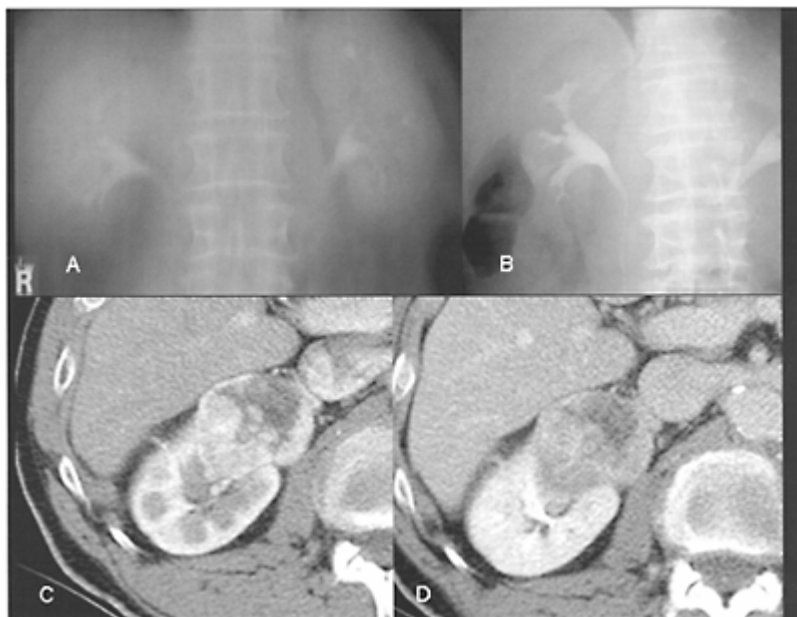


**Figure 6.4** (A) Selected image of right kidney from an IVP obtained for microhematuria in a 45-year-old male. (B–D) Subsequent CT images show lower pole 2 cm renal cell mass. Lesion was not appreciated on IVP.

CT has been established as the most sensitive and specific modality in the detection and staging of RCCa.<sup>10–13</sup> Indeed, the ubiquitous use of CT scanners in the United States for diagnosis of various complaints has led to an artificial increase in the incidence of RCCa.<sup>14,15</sup> From 1935 to 1965 only 7% of RCCa were found incidentally, 13% from 1961 through 1973, 48% from 1980 through 1984, with now 60–81% being discovered incidentally.<sup>14,16–18</sup> Due to the advances in imaging, up to 38% of lesions are now detected when they are 3 cm or less in size.<sup>11</sup> Such early detection has seemingly led to an improvement in survival, although lead time bias may play a role. Thompson et al found that 90% of patients with incidentally discovered tumors were alive at 10 years, vs

only 30% of patients with symptomatic tumors.<sup>19</sup> Such early detection has also expanded the options for patients as regards radical nephrectomy vs open nephron-sparing surgery vs laparoscopic radical or partial nephrectomy. Patients with lowgrade, small (i.e. <4 cm) tumors having nephron-sparing surgery seem to have an outcome equivalent to that obtained via radical nephrectomy.<sup>20</sup>

At our institution we evaluate all adult patients referred with hematuria using a combination of helical triphasic CT and IVP (Table 6.2). To summarize, patients have a routine KUB (kidney, ureter, and bladder) performed, followed by noncontrast CT through the abdomen and

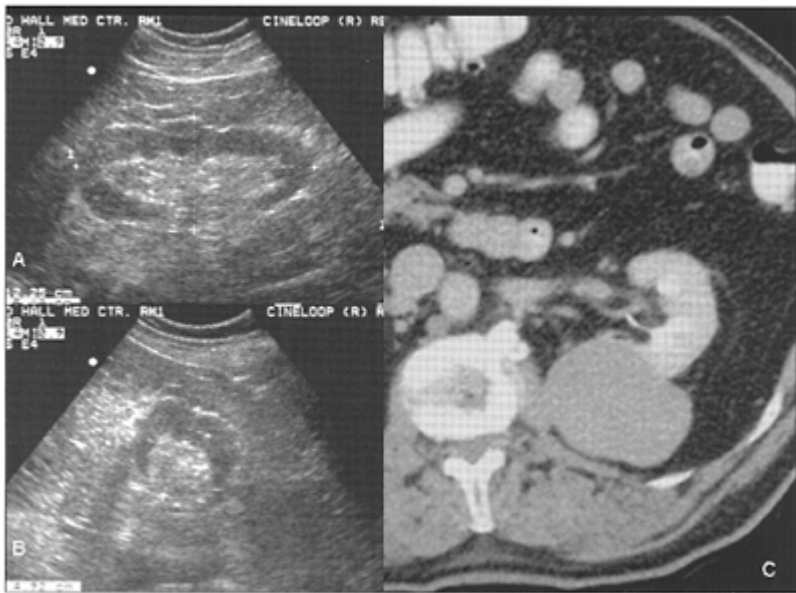


**Figure 6.5** (A and B) Selected images obtained from IVP performed in a patient with microhematuria. (C and D) Subsequent CT images demonstrate large mass arising from medial upper pole of right kidney. Note that this large lesion is not readily apparent on the IVP.

pelvis, followed by image acquisition during a corticomedullary phase at 90 s after contrast injection to assess the parenchyma, followed by an excretory delayed phase at 5 min to assess the collecting system. The last phase is also obtained from the top of the kidneys through the entire abdomen and pelvis. After the last phase there is excellent opacification of the collecting system and a compression device is applied to the lower

abdomen. The collecting system is thus distended and the patient removed to the routine radiography suite for anteroposterior (AP), prone, and oblique views to assess the ureters and finally a postvoid image of the pelvis. Each request is reviewed by a radiologist days in advance, with the protocol being easily adaptable for the question to be answered. The nephrographic phase demonstrates the highest sensitivity for parenchymal lesion detection, whereas the corticomedullary phase is best for assessing the renal vasculature and surrounding organs for metastatic disease or coexisting pathology.<sup>21</sup>

The use of helical CT allows high resolution due to rapid acquisition of the images.<sup>12</sup> First, each phase of the CT portion of the protocol can be obtained in a standard single breath hold, which is comfortable for the majority of patients. This minimizes misregistration between individual slices due to respiratory variation. Also, each phase can thus be obtained with a similar breath-hold maneuver, which allows a slice-by-slice comparison as regards enhancement of any lesion being assessed (Figure 6.7). Such comparison is facilitated by use of a multipanel computer workstation (PACS—picture acquisition and communication system) (Figure 6.8), which allows side-by-side evaluation of each phase. The radiologist can also



**Figure 6.6** (A and B) Longitudinal and transverse ultrasound images of left kidney obtained in a patient with microhematuria. (C) Correlating CT image demonstrates large left renal mass. Mass was not initially appreciated on US.

apply region of interest (ROI) boxes of any desired size to assess relative attenuation—application of Hounsfield units (HU)—of the tissues, pre- and post-contrast.

### Renal masses: cystic and otherwise

Fortunately, the majority of renal ‘masses’ are not malignant.<sup>11</sup> The differential diagnosis includes benign cysts, angiomyolipoma, lymphoma, metastases, oncocytomas, abscesses, and hematomas. History and ancillary studies may help narrow the diagnosis in the particular patient. Simple renal cysts are extremely common, being seen in over half of the population over the age of 50 years.<sup>22</sup> CT criteria for a simple benign cyst include:

1. sharp margination with the surrounding renal parenchyma
2. no perceptible wall
3. homogenous attenuation near water density (−10 to 15 Hounsfield units)
4. no enhancement after administration of contrast.<sup>23</sup>

Indeterminant cystic masses may represent cystic RCCa, or a simple cyst that has been complicated by infection or hemorrhage (Figure 6.9). A cyst cannot be assessed as simple if:

1. there is a perceptible wall with either regular or irregular thickening of the wall
2. solid components within a cystic mass
3. enhancement of the wall or septations
4. irregular margins
5. inhomogeneous cyst fluid.

However, cysts which are <3 cm which have high attenuation values, commonly termed ‘hyperdense’ cysts, may be considered benign provided that other criteria of

**Table 6.2** *CT/IVP protocol*

Position: supine

Scout: AP

Pitch: 1.5

KVP: 120

MA: 250

Rotation time (s): 1

Injection rate: 2 ml/s

IV contrast: 125 ml non-ionic

|                 | Phase 1 (NONCON) | Phase 2 | Phase 3 |
|-----------------|------------------|---------|---------|
| Slice thickness | 5 mm             | 5 mm    | 5 mm    |
| Slice increment | 5 mm             | 5 mm    | 5 mm    |
| Scan delay      | N/A              | 90 s    | 5 min   |
| Scan area       | ABD/PLV          | KIDS    | ABD/PLV |

Scanogram (topogram of ABD/PLV after the 90 s and 5 min scans).

Compression applied to lower abdomen immediately after 5 min scan and patient taken to standard radiography suite for completion of IVP portion of examination.

Assumes single-detector helical system with pitch=distance couch moves during one revolution of the X-ray tube.

simplicity are met, most notably lack of enhancement.<sup>23</sup> Approximately one-third of RCCs are hyperdense relative to the surrounding parenchyma on noncontrast CT.<sup>24</sup> A lesion with CT characteristics suggesting a hyperdense cyst may be further evaluated with ultrasound, in which 50% will meet criteria of a simple cyst.<sup>25</sup>

In 1986 Bosniak proposed a classification system of renal cystic lesions to allow stratification into management groups. Category 1 includes the purely simple cyst in which no further management is necessary unless symptomatic due to pure mass effect. Category 2 comprises minimally complicated cysts in which there are fine septations and minimal wall (i.e. rim) calcifications. This category includes hyperdense cysts. Category 3 comprises moderately complicated cysts that cannot be dismissed as benign by radiologic studies. Such lesions may be grossly hemorrhagic, have thick septations, dense calcifications, etc. As these lesions cannot be safely characterized as benign, excision is mandatory (Figure 6.10). Category 4 implies cystic RCCa until proven otherwise.<sup>26</sup> Finally, a last category, 2F, was devised, comprising minimally complicated cysts that require follow-up. This 'gray zone' between categories 2 and 3 is left to the judgment of the radiologist in concert with the urologic surgeon. Stability implies benignity, and such patients should be monitored with repeat studies at 3 months, 6 months, and 1 year.<sup>25</sup> Subsequent yearly monitoring out to 5 years would seem an acceptable and conser-



**Figure 6.7** Three-phase CT as part of CT-IVP, demonstrating co-registration

of images in noncontrast (A), nephrogram (B), and excretory phases (C).

vative extension to this regimen. Prolonged monitoring of a suspicious lesion must take into account the concerns of the patient, and the reliability of the patient as regards return for follow-up.

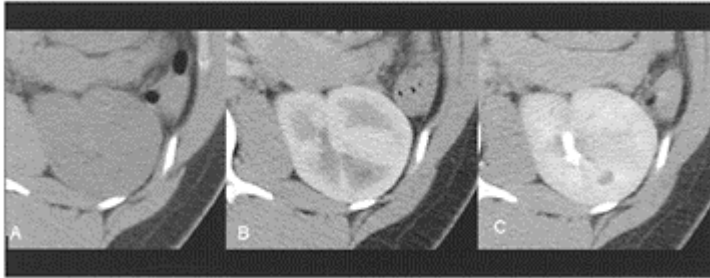
The use of, and reliance upon, the Bosniak classification must be tempered with an understanding of the limits of interobserver variability. Siegel et al demonstrated in one series that 16% of lesions thought to be Bosniak category 1 or 2 by one radiologist were upgraded by a another radiologist to category 3 or 4.<sup>27</sup> Based upon pathologic verification, the incidences of malignancy in this series correlated to the respective categories and were 0%, 13%, 45%, and 90%.

Non-RCCa masses include angiomyolipomas (renal hamartoma), metastatic disease, and lymphomas, either primary or secondary. The sine qua non of radiologic diagnosis of angiomyolipoma (AML) is the presence of macroscopic fat within the lesion (Figure 6.11). Ninety percent of AMLs have sufficient fat to make the diagnosis on CT, with the remainder termed angiomyomas as they lack the lipomatous component.<sup>28</sup> Twenty percent of patients with



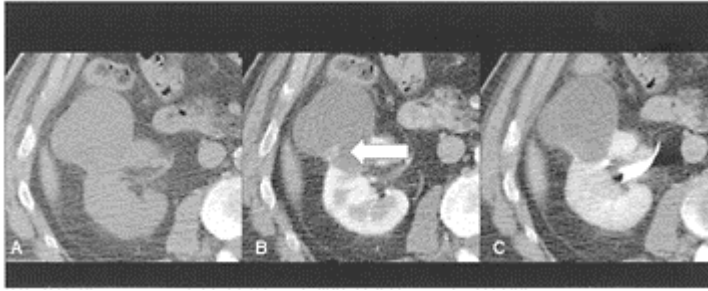
**Figure 6.8** PACS (Picture archiving and communication system) workstation. A computerized workstation facilitates direct comparison between phases of triphasic CT during CT-IVP. The system allows rapid scrolling through

images. Note that the far right panel may be used to correlate IVP images with CT images on other panels.

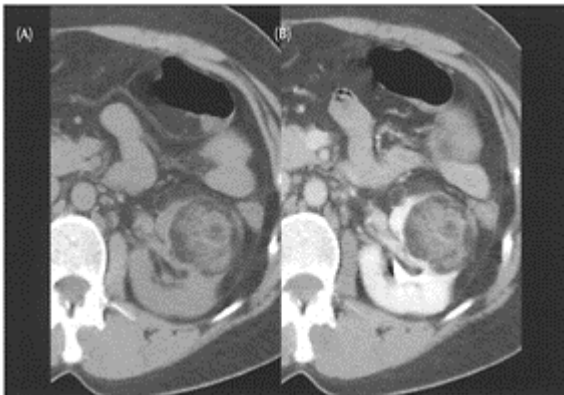


**Figure 6.9** CT-IVP small renal cell carcinoma. A 35-year-old male with persistent microhematuria had negative evaluation with IVP and cystoscopy several months before. Repeat evaluation with triphasic CT demonstrates small lesion that is inconspicuous on noncontrast image (A), but is identified on the nephrogram/cortical phase (B), and excretory phase (C). The lesion, removed with partial nephrectomy, was a small renal cell carcinoma.

AML, predominantly males, suffer from tuberous sclerosis, a phakomatosis characterized by the constellation of adenoma sebaceum of the face, cerebral cortical tubers predisposing the patient to seizures, mental retardation, and giant cell astrocytomas.<sup>29</sup> However, 80% of cases, predominantly middle-aged women, have sporadic AMLs that are not related to any syndrome. The predominant clinical manifestation of AML is hemorrhage, with the risk increasing markedly after a size of 4 cm is reached.<sup>30</sup> While histologically benign, AMLs do grow over time, with up to 50% of AMLs <4 cm and 75% >4 cm demonstrating growth over a 4-year period.<sup>31,32</sup> Seventy percent of patients eventually become symptomatic once tumor size exceeds 4 cm; 20% of patients present in shock due to



**Figure 6.10** Cystic renal cell carcinoma. A 48-year-old patient with microhematuria. A noncontrast image (A) suggests the presence of a simple cyst, arising from anterior surface of the right kidney. Nephrographic (B) and excretory (C) phases demonstrate a nodule (arrow) within the cyst as well as enhancement of a septum. It was classified as a Bosniak category 3 lesion, and exploration revealed a cystic renal cell carcinoma.



**Figure 6.11** Angiomyelolipoma. A 34-year-old female presented to the emergency department, complaining of left flank pain. Noncontrast CT (A) was requested to rule out ureteral



calculus. Incidental finding of angiomyelolipoma. Note the macroscopic fat within the lesion in comparison to retroperitoneal fat. (B) Contrast enhanced CT at the same level.

hemorrhage.<sup>33</sup> Once diagnosis is made for those tumors less than 4 cm, a period of yearly observation, via ultrasound, is recommended. For those patients with tumors greater than 4 cm, excision should be considered, or, if comorbidity prohibits surgery, transcatheter angiographic embolization is an option.<sup>34</sup>

Metastatic disease to the kidney, while often not symptomatic, is sometimes discovered due to the frequent CTs cancer patients receive. The most common lesion is secondary to a lung primary. Metastases to the kidney can be expansile and 'ball' shaped or infiltrative, a pattern seen in squamous cell carcinomas and lymphomas.<sup>35</sup> Additionally, infiltration of renal pelvic transitional cell carcinoma into the parenchyma needs to be considered (Figure 6.12). Usually there is a history of a primary malignancy, and, if the renal lesion seems to be the only lesion present, consideration should be made regarding biopsy so the proper therapy is rendered. However, in the majority of patients with a history of malignancy who have an isolated renal lesion the pathology will reveal primary RCCa.<sup>25</sup> Lymphoma, while predominantly infiltrative, can also present as a solitary renal mass or diffuse involvement of both kidneys. The most common lymphoma to involve the kidneys is of the non-Hodgkin's variety. Lymphoma may



**Figure 6.12** Transitional cell carcinoma infiltrating the kidney. A 68-year-old male with a history of prior muscle invasive bladder transitional cell carcinoma with gross

hematuria from ileal conduit diversion. This CT image with contrast reveals diffuse infiltration of renal parenchyma (arrow) with disease that has already filled the collecting system. Note that primary or secondary renal lymphoma can have a similar appearance.

also involve the perirenal space, with direct spread from primary retroperitoneal disease.<sup>35</sup> Bulky retroperitoneal adenopathy with an infiltrative renal lesion suggests the diagnosis.

### **Use of magnetic resonance imaging**

MRI in the evaluation of the renal mass for the most part is not necessary given the advances in CT technique. However, MRI is a consideration for those patients with an allergy to iodinated contrast or with pre-existing renal insufficiency which may be worsened with a contrast load. This is of special import in those patients that have had prior nephrectomy and are now faced with a metachronous lesion of the remaining kidney. The immediate advantage of MRI is in multiplanar imaging and in assessment of venous involvement (Figure 6.13).<sup>36</sup> Additionally, gadolinium contrast may be used with safety in patients with renal insufficiency and has an extremely low risk of inducing an allergic response.<sup>37</sup>

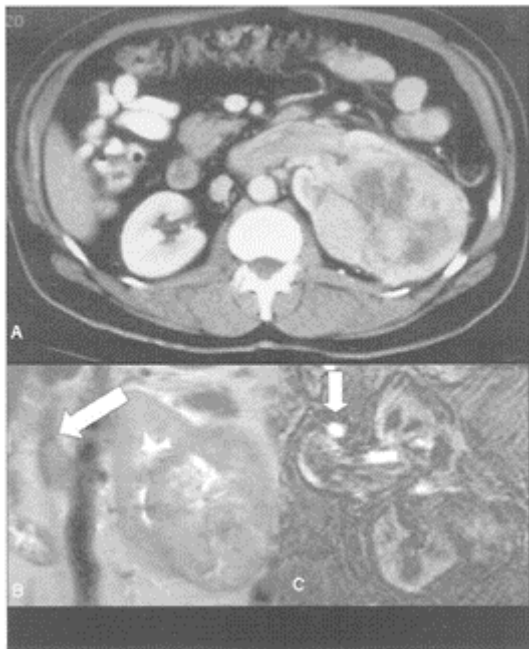
As with CT, simple cysts should be well circumscribed, with homogenous decreased signal intensity on T1-weighted imaging and increased intensity on T2 (usually isointense to the cerebrospinal fluid (CSF) in the spinal canal, a useful internal reference for comparison). Hemorrhagic cysts will demonstrate variable T1-signal intensity, depending upon the protein content of the fluid and/or the age of the hemorrhagic components in the cyst. Similar variability is also seen on T2-weighted images. With continued evolution, hemorrhagic cysts become of low signal intensity in both T1 and T2 as the hemoglobin within the cyst breaks down and eventually becomes replaced with hemosiderin. Wall calcification in a cyst is poorly appreciated by MRI. The principal criterion of differentiation between a benign complex cyst and a cystic neoplasm is lack of enhancement of the former entity. However, some benign lesions will demonstrate variable enhancement with gadolinium, to include traumatic hematomas, infectious processes such as infected cysts and abscesses, and xanthogranulomatous pyelonephritis.<sup>38</sup> Again, clinical history is indispensable in this regard.

While considerable variability exists, RCCa appears heterogeneous on T1-weighted sequences and becomes hyperintense on T2-weighted sequences.<sup>39</sup> However, some investigators have abandoned T2-weighted images in their 'renal mass' protocols as it is felt that lesion characterization with this pulse sequence is not necessary for a solid mass.<sup>40</sup> Instead, reliance is on rapid T1-weighted gradient echo (GRE) sequences with fat suppression. T2-weighted images require several seconds for acquisition, whereas T1-GRE images can be obtained in milliseconds. Such rapidity allows minimization of

motion-related artifacts due to breathing or vasculature pulsation. Fat-suppressed images also assist in evaluating the perirenal space for involvement. Evaluation of indeterminant lesions may be evaluated with T1, T2 (still useful, in our opinion, for cystic lesions), and T1-GRE fat-saturated post-gadolinium contrasted images, again with the determination of possible malignancy based upon enhancement. However, due to the expense of MRI, in the absence of the contraindications above, it is recommended that most patients be evaluated with dynamic enhanced CT due to its wide availability and accuracy.<sup>36</sup>

### Multidetector computed tomography

While, as discussed above, the IVP has limitations assessing parenchymal lesions, it remains the mainstay of assessing the collecting system and ureters. Recently, however, the use of multidetector CT (MDCT) has begun to challenge the seeming monopoly on the collecting system that IVP has held for decades. The majority of helical CT scanners in use in the United States are currently those employing single-detector technology. A single spiral or helical plane of data is generated with each rotation of the X-ray tube and detector as the patient is moved through the gantry.<sup>41</sup> The images eventually created at each axial plane are



**Figure 6.13** Tumor thrombus. A 56-year-old male presenting with asymptomatic gross hematuria.

Contrast CT (A) reveals a large left renal mass with markedly engorged left renal vein. This T2-weighted coronal MR image (B) suggests the presence of a tumor thrombus just within inferior vena cava (arrow). A gradient recall image (C) confirms the thrombus within the left renal vein, extending into the inferior vena cava (IVC) (arrow on superior mesenteric artery origin).

actually *an estimate*, or interpolation, of the information (specifically of the portions of the patient between the helical imaging ‘slices’) that would have been obtained had the gantry made an entire revolution at each particular axial position (the ‘old’ stop and image in each plane method). Slice thickness is determined by the collimation of the X-ray beam before imaging acquisition. With MDCT, multiple helical scan planes are obtained simultaneously and slice thickness is determined by the configuration of the detector row and the pre-selected X-ray beam collimation. To use a simplified example, with a 4 detector bank, 4 times the information is obtained (4 times the number of slices) with a single pass through the scanner compared to a single detector system in the same amount of time. Consequently, more refined post-acquisition image reconstruction can be done, in any plane, with very little loss of resolution, as the originally imaged planes obtained overlap. Additionally, post-acquisition slice thickness reconstruction can be done down to the size of the smallest detector without having to re-scan the patient and reset the beam collimation. The amount of information acquired not only allows multiplanar reconstruction but also allows smooth 3D volume-rendered images to be reconstructed. This is of benefit in situations where detailed imaging of vascular anatomy is requested prior to minimally invasive surgery such as with living related renal donors and correction of ureteropelvic junction obstruction.<sup>21,42,43</sup> Evaluation of such patients is discussed later in this chapter.

### Computed tomographic urography

Three types of ‘CT urography’ have been described:

1. standard axial CT, with scout images of the abdomen (the ‘scanogram’) pre- and post-contrast using the CT scan dataset obtained during axial acquisition
2. hybrid examinations that combine CT and IVP (used at our institution)
3. MDCT with subsequent 3D reconstructed images in the coronal plane from the data set.<sup>44</sup>

For those institutions with MDCT technology, complete imaging evaluation of the urinary tract may be performed in the CT suite. Reportedly, there is no significant

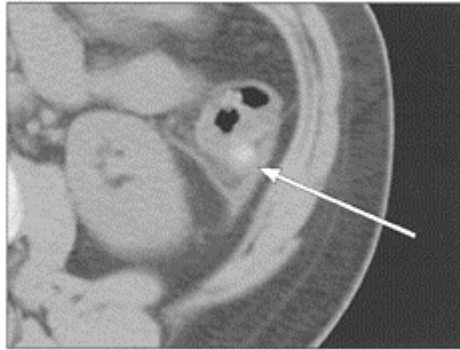
difference in the opacification of the collecting system as regards conventional urography and reconstructed MDCT urography.<sup>45</sup> However, there has yet been no comparison of MDCT urography with conventional urography as regards small-volume upper-tract urothelial (i.e. transitional cell carcinoma) disease. MDCT urography does have utility, however, in localizing urolithiasis, defining collecting system anatomy and anomalies, and assessing intravesicle pathology.<sup>46</sup> The use of MDCT urography to produce detailed images of the bladder has led to 3D reconstructed images yielding the so-called 'Virtual cystoscopy'. While polypoid lesions are ideal for detection with the 3D reconstructed images, detection of bladder wall thickening requires detailed assessment of the axial views. Recently reported, however, is a series in which 88% of bladder urothelial lesions less than 0.5 cm in size were detectable with an overall sensitivity and specificity of 95 and 87%, respectively.<sup>47</sup> While MDCT may demonstrate ureteral obstruction and narrowing, concentric wall narrowing due to urothelial disease is not well appreciated on the reconstructed images, whereas with standard urography small mucosal abnormalities that may indicate a need for ureteroscopic evaluation may be easily detected.<sup>44</sup> Using a phantom, screen-film systems and computerized radiography have been demonstrated to maintain higher resolution in regards to line pairs per millimeter, whereas CT offers better contrast discrimination.<sup>48</sup> Although this is a technology that is in evolution and will, no doubt, improve, several investigators feel that due to limitations in spatial resolution MDCT urography has not yet reached a point where the standard intravenous urogram can be abandoned.<sup>49-51</sup> The main advantage of MDCT urography at this point is the ability to obtain a complete imaging package with 'one' study, i.e. the patient has just the CT and does not require movement to another room for subsequent radiographic imaging.

### **Noncontrast computed tomography in evaluation of renal colic**

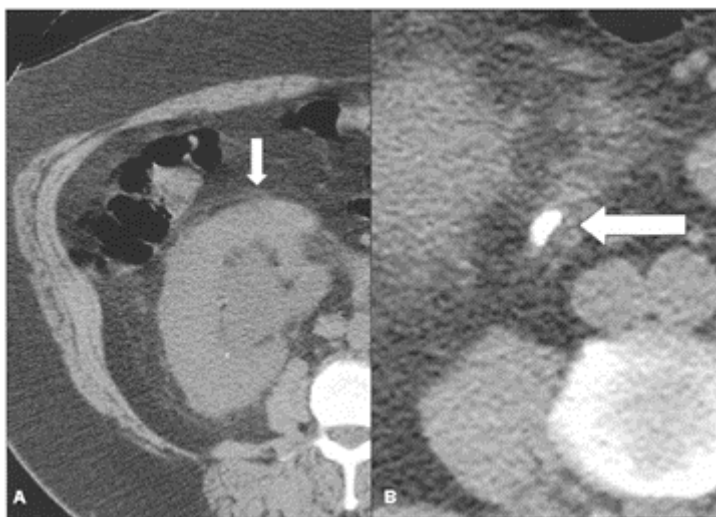
Intravenous pyelogram/urography has ceded superiority to unenhanced helical CT (UHCT) in the diagnosis of acute renal colic due to ureterolithiasis. This paradigm shift began with the publication of Smith et al regarding direct comparison of UHCT with what was then the gold standard, IVP.<sup>52</sup> The efficacy of CT in this regard was further demonstrated by the study being terminated after only 22 patients when CT was found to be the profoundly more accurate modality. Advantages of UHCT included rapid acquisition of images, no need for contrast, lower dose of radiation (compared to IVP), and the ability to diagnose other causes of flank pain.<sup>53</sup> Disadvantages were misdiagnosis of urolithiasis due to surgical clips or pelvic phleboliths. A recent review of the world literature regarding UHCT for renal colic reveals the sensitivity and accuracy for calculus identification and diagnosis ranges from 94 to 100% and from 93 to 98%, respectively.<sup>54</sup> About 10% of patients thought to have a ureteral calculus were found in one series to have an alternative diagnosis which was felt to be the etiology of the patient's flank pain.<sup>55</sup> Thus, UHCT was felt to be a useful screening tool that allowed triaging the patient to either optimal therapy, or selection of additional imaging to further elucidate the problem (Figure 6.14).

Occasionally, identification of the actual calculus may be difficult, either due to small size, or the patient may be imaged immediately after stone passage. Additionally,

calcification in the pelvis may be due to venous phleboliths or atherosclerotic disease. Thus, secondary signs of obstruction/inflammation are also of import in UHCT. Definitive identification of a ureteral stone is thought to require the calcification to have a surrounding rim of tissue—the edematous ureteral wall (Figure 6.15)<sup>56</sup> However, the so-called ‘rim sign’ is only observed in 50–80% of patients, and 8% of phleboliths may also have a soft tissue rim.<sup>57,58</sup> Attenuation of the calcification is also helpful, as in one series it was found that if the calcification had an attenuation of more than 311 Hounsfield units the probability of it being a phlebolith was only 0.03%.<sup>59</sup>



**Figure 6.14** Diverticulitis. A 19-year-old female presenting to the emergency room with complaint of left flank pain was found instead to have diverticulitis of the descending colon. Note the surrounding inflammation and presence of a fecalith in the infected diverticulum (arrow).



**Figure 6.15** NECT (nonenhanced CT) for renal colic. A 55-year-old female presenting to emergency department with complaint of right flank pain. (A) NECT demonstrates an enlarged hydronephrotic right kidney with perinephric stranding (arrow). (B) Magnified image of proximal ureter demonstrates a calculus obstructing the ureter with surrounding soft tissue density, the ‘rim’ sign.

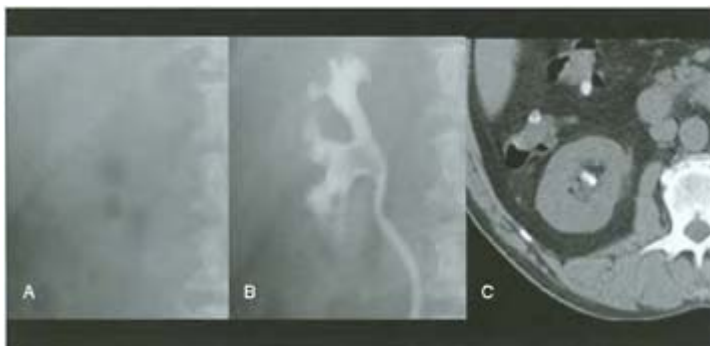
Hydronephrosis proximal to the stone is seen in almost 70% of patients, with perinephric stranding in 65% of patients (Figure 6.15).<sup>60</sup> Combination of unilateral hydronephrosis or ureteral dilatation with ipsilateral perinephric or periureteral stranding in one series had a positive predictive value of 98%.<sup>61</sup> absence, thereof, had a negative predictive value of 91%. Additionally, stones that are not readily seen by plain radiography are easily seen via unenhanced computed tomography (UECT) (Figure 6.16).

Rarely, the use of contrast may be required to make the definitive diagnosis. Older and Jenkins have proposed a management schema outlining UHCT findings and further diagnostic evaluation:<sup>56</sup>

1. Secondary signs positive: hydronephrosis and/or perinephric fluid, and definite stone (rim sign) or very likely stone in ureter. Diagnosis: ureteral stone—no contrast needed.
2. Secondary signs positive: hydronephrosis and/or perinephric fluid, and no ureteral stone definitively seen. Diagnosis: the stone has probably passed—no contrast needed.

3. Secondary signs negative: no hydronephrosis or perinephric fluid, but definitive stone in ureter on side of flank pain (rim sign present). Diagnosis: ureteral stone—no contrast needed.
4. Secondary signs positive: hydronephrosis and/or perinephric fluid and probable stone in ureter. Diagnosis: ureteral stone—no contrast needed.
5. Secondary signs negative: no hydronephrosis or perinephric fluid, and no suspicious calcification. Diagnosis: no ureteral stone—no contrast needed.
6. Secondary signs negative: no hydronephrosis, no perinephric fluid; possible ureteral stone, but not definite. Diagnosis: indeterminant—contrast needed.

In the sixth scenario, definitive evaluation may be made by intravenous pyelography or retrograde pyelography. The advantage of the latter is that the urologist may immediately manage or temporize the problem with ureteroscopic removal or placement of a ureteral stent if felt to be clinically necessary. The CT protocol for renal colic used at our institution is provided in Table 6.3. Note that the patient may be scanned in the prone position to discriminate calculi that have passed into the bladder from those that remain lodged in the ureterovesical junction (Figure 6.17).



**Figure 6.16** Radiolucent stone. (A) Coned down scout image of right renal fossa in a KUB obtained prior to retrograde pyelogram for gross hematuria in a 45-year-old male. (B) Coned down image obtained from retrograde pyelogram demonstrating radiolucent filling defect in renal pelvis. (C) Noncontrast CT reveals unsuspected calculus composed of uric acid. Retained enteric contrast in several colonic diverticula are also seen.



**Table 6.3** *CT abdomen/pelvis (noncontrast) for urinary calculi*

Position: prone (allows any stones in posterior bladder to fall forward)

Scout: PA

Scan area: from just above diaphragm through symphysis pubis

Slice increment: 5.0 mm

Slice thickness: 6.5 mm

Field of view: varies with patient size

Pitch: 0.875

Rotation time (s): 0.75

KVP: 120

mA: 200–300

Algorithm: standard

Breath hold: 25–30 s inspiration

Assumes single-detector helical system with pitch=distance couch moves during one revolution of the X-ray tube.

**Preoperative evaluation of ureteropelvic junction obstruction in adults**

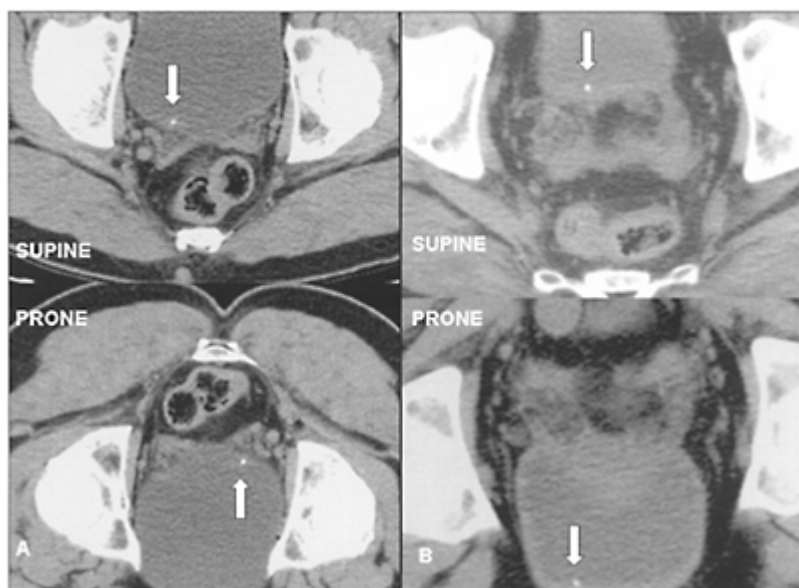
The three goals of imaging of possible UPJO are:

1. determination of the presence and degree of renal obstruction
2. determination of residual renal function
3. determination of the cause of the obstruction.<sup>62</sup>

The most common complaint is pain, either constant or pyelonephritis are also significant presenting signs.<sup>63</sup> Further evaluation may then be made with IVP, diuretic nuclear renography, retrograde pyelography, and a provocative assessment of intrapelvic pressures, the Whitaker test.<sup>64</sup>

After presenting symptoms and initial imaging suggest the possibility of UPJO, most authors state reliance upon diuretic nuclear renography for assessment of residual renal function and degree of obstruction due to the relative noninvasiveness of the test.<sup>62</sup> The agents used currently are technetium 99m diethylenetriamine pentaacetic acid (Tc99m-DTPA) and technetium 99m mercaptoacetyltriglycine (Tc99m-MAG-3), with the former being predominantly excreted by glomerular filtration, the latter predominantly by tubular secretion. Tc99m-MAG-3 is currently felt to be the agent of choice as it is much less affected by impaired glomerular filtration, which may be significant in chronically obstructed kidneys.<sup>65</sup> Initial imaging, specifically the first 1–2 min after radiopharmaceutical injection, demonstrates renal blood flow and processing of the radiopharmaceutical through the parenchyma, thus assessing function. The peak cortical uptake of radiopharmaceutical in the obstructed side may be delayed, with the maximum parenchymal uptake rarely reaching that of the normal side. Filling of the collecting system is likewise delayed. However, due to the capacity of the dilated renal pelvis, the maximum activity in the affected collecting system frequently exceeds the normal side

long after the normal side has cleared the radiopharmaceutical.<sup>66</sup> Usually, furosemide (40 mg) is administered either after a preset time during the protocol (15–30 min

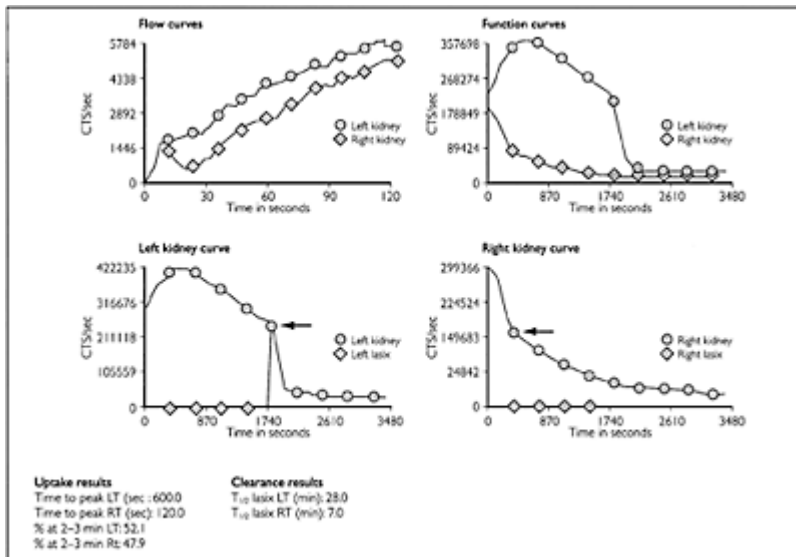


**Figure 6.17** Effect of positioning in patients undergoing NECT (nonenhanced CT) for renal colic. Patients are placed in the prone position routinely. (A) A patient with a calculus at the ureterovesical junction, confirmed with stone remaining in position while prone. (B) Another patient with a posterior calculus, which, when in the supine position, may be trapped at the ureterovesical junction. In the prone position the stone is seen to fall forward, confirming that the stone is intravesical.

after radiopharmaceutical injection) or, more appropriately, after the collecting system on the obstructed side has reached maximum activity. In an obstructed system, washout of radiopharmaceutical from the collecting system is either unchanged with diuretic administration or significantly blunted. Quantification is done by calculating a  $T_{1/2}$

value—the time that half the activity is lost from the drawn region of interest. While  $T_{1/2}$  standards were first formulated in the pediatric population, most clinicians agree that a  $T_{1/2}$  of less than 10 min indicates no significant obstruction, 10–20 min is equivocal, and more than 20 min is strongly suggestive of obstruction (Figure 6.18).<sup>67</sup>

False-positive results may occur in patients that are inadequately hydrated and may arise with kidneys that are extremely compromised and thus not able to respond adequately to furosemide (or due to an inadequate dose being given). Failure of the collecting system to fill with radiopharmaceutical within 1 hour or ipsilateral function less than 20% of total renal function virtually guarantees prolonged excretion, even without significant obstruction. Also, induced diuresis may fail to clear a system of very large capacity. Finally, a *normal* kidney without any collecting system retention will produce a  $T_{1/2}$  of greater than 20 min; thus, furosemide should not be administered unless radiopharmaceutical is demonstrated to be retained in the renal pelvis or ureter.<sup>68</sup> A false positive may be seen in over 10% of patients, even when no significant obstruction exists.<sup>62</sup> Despite limitations, with attention to technique and appropriate pre-study hydration, the incidence of a false-negative study is very low (<1%).<sup>69</sup> Studies that are discordant with other imaging studies, or the patient's symptoms, should be either repeated, or consideration given to performing a perfusion pressure, or Whitaker test. The Whitaker test does require percutaneous access of the collecting system, limiting enthusiasm for its use. Also, accumulated experience with diuretic nuclear renography



**Figure 6.18** Diuretic renography.  
Tc99m-MAG-3 diuretic renogram in a 30-year-old female with symptomatic left ureteropelvic junction obstruction. Furosemide is administered

intravenously when the collecting systems have reached maximum counts and  $T_{1/2}$  calculated when counts in the collecting system reach half-maximum (black arrows). In this case the  $T_{1/2}$  for the symptomatic left kidney is 28 min, which is indicative of significant obstruction.

has also made the Whitaker test a modality that is now infrequently used. A discussion on the role of the Whitaker test in the evaluation of UP JO is found in Chapter 13.

Once physiologic evidence of obstruction is established, anatomic imaging serves in selecting the operative modality that would best serve the patient. Specifically, the questions to be answered are:

1. How much residual function remains in the obstructed kidney or, more to the point, would the patient be better served with a nephrectomy?
2. Are there any stones in the collecting system? Is there a need for concomitant percutaneous or ureteroscopic stone removal?
3. What is the vascular anatomy of the kidney? How does it relate to the obstruction? How will the anatomy affect the modality selected?

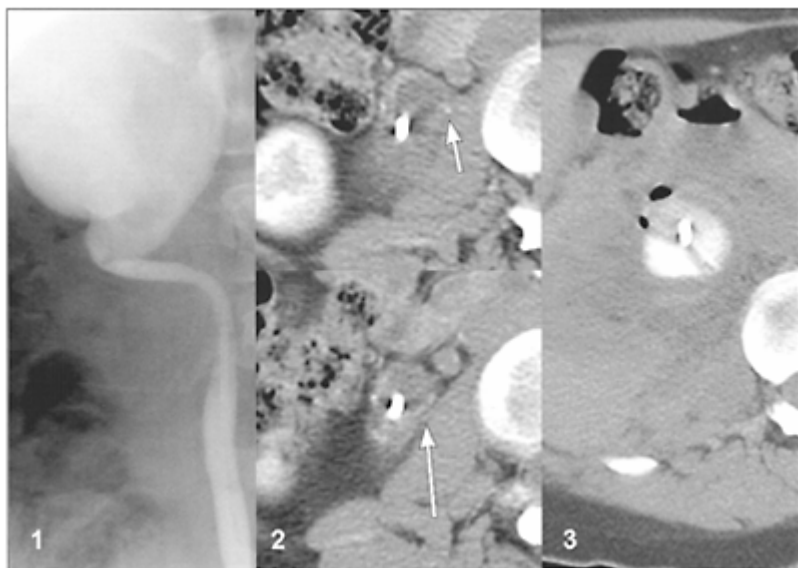
During the diuretic renogram care is taken to draw the ROI area only over the renal parenchyma and not to include the area of the collecting system.<sup>70</sup> Also, as above, functional imaging is obtained in the first 1–2 min for MAG-3 to avoid a spurious overassessment of functionality due to excretion into the collecting system. Each kidney, in the normal state, contributes between 45 and 55% of the total nephron mass/function. Poor renal function does play a role in the success of relief of UP JO by endoscopic/endourologic means. Success rates from antegrade pyelotomy in one large adult series were found to decrease from 92% to 54% when preoperative function in the affected kidney was less than 25%.<sup>71</sup> This has also been confirmed in the pediatric population, although such a decrease in success is not reported for open dismembered pyeloplasty.<sup>72</sup> Nakada and coworkers have recommended 20% function as a decision point in adults and also recommend a period of percutaneous drainage to allow any residual function to return prior to making a decision for nephrectomy.<sup>64,73</sup> Should diuretic renography be equivocal and a period of percutaneous drainage considered, a Whitaker test may be easily accomplished.

Calculi are present in the setting of UP JO in approximately 20% of patients.<sup>63</sup> Inflammation within the renal pelvis due to calculus disease may play a role in the etiology of the UPJO, although this is felt to be more a theoretical concern as no studies exist to suggest direct causation of submucosal fibrosis.<sup>74</sup> However, if a calculus is impacted at the site of the UPJO or has been so, there is some evidence to suggest that success of pyelotomy may be compromised due to underlying scarring.<sup>75</sup> Indeed, if a calculus was impacted at the UPJ, consideration may be given to stone removal and then reassessment of residual obstruction after a period of ureteral stenting and removal. However, non-impacted stones should be treated simultaneously with management of the

UPJO to allow the patient to be managed with one procedure if at all possible.<sup>64,74</sup> Given the previous discussion as regards superiority of UHCT in the diagnosis of urolithiasis, any suspicion of a coexisting calculus may be assessed by that modality.

While in the pediatric population UPJO seems to be more related to intrinsic smooth muscle deficiency, the etiology of adult UPJO seems less well established.<sup>76</sup> Confounding the intrinsic muscular deficiency etiology in adults is the relatively late presentation in some patients, cognizant that such muscle deficiency should have become manifest in childhood.<sup>77</sup> There is, however, compelling evidence of the role of vessels crossing the ureter either at or in close proximity to the UPJ. In a study of several hundred cadaver kidneys, Sampaio found large arteries or veins ventrally to the UPJ in 65% of kidneys, with 45% of UPJs being found in close proximity to the inferior segmental artery.<sup>78</sup> Inferior polar arteries (arteries directly entering the parenchyma, not the hilum) were found in 6.8%, and in 6.2% there was a dorsal artery in close relation to the UPJ. The majority of these polar arteries arise directly from the aorta. The incidence of a crossing vessel in adults with UPJO is from 50 to 80%.<sup>77,79</sup> In many cases it may be a direct cause of the obstruction; in others the aberrant vessel may be merely an innocent bystander. The vessel may exacerbate the problem as the dilated renal pelvis may, over time, drape over the vessel and compound the pre-existing obstruction.<sup>80</sup>

The initial implication of the crossing vessel seems to be decreased success with endopyelotomy; however, post-operative hemorrhage and segmental parenchymal infarction are also important considerations (Figure 6.19). Accordingly, some authors have proposed that patients



**Figure 6.19** Crossing vessel on CT and postoperative hemorrhage. (1) A 24-year-old female with symptomatic

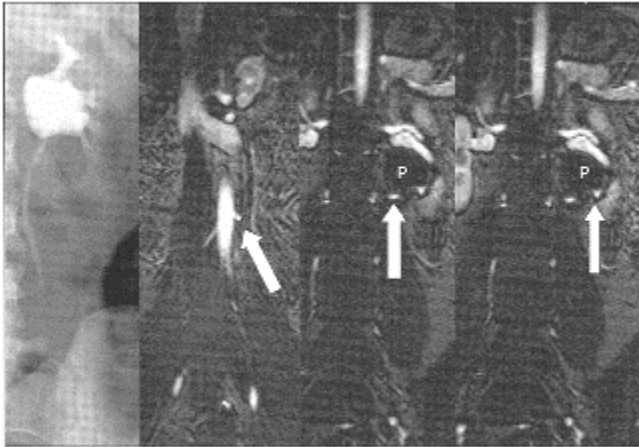
left-sided ureteropelvic junction obstruction. (2) Contrast-enhanced CT demonstrates a small vessel abutting the area of the obstruction and passing anterior to it. This vessel was not recognized preoperatively. A ureteral stent is in place across the obstruction. (3) After endoscopic endopyelotomy, there is a large perinephric hematoma secondary to transection of this vessel.

with crossing vessels be offered open or laparoscopic pyeloplasty instead of endoluminal techniques such as endoscopic pyelotomy. Van Cangh et al found that the success rate of endopyelotomy was only 33% with a crossing vessel, vs 82% in those patients without.<sup>81</sup> Assessment of the perirenal vascular anatomy would seem essential regarding successful treatment of UPJO. A large inferior segmental artery or small parenchymal branch may play a role in the etiology of the UPJO, and may be problematic for endourologic treatment. Such a patient may require selection for laparoscopic or open pyeloplasty and thus may be appropriately counseled.<sup>80,82</sup> Vessels that cross the ureter within 1.5 cm of the UPJ are usually anterior; thus, most urologists, when performing endoscopic pyelotomy, make the ureteral incision posterolaterally.<sup>79</sup>

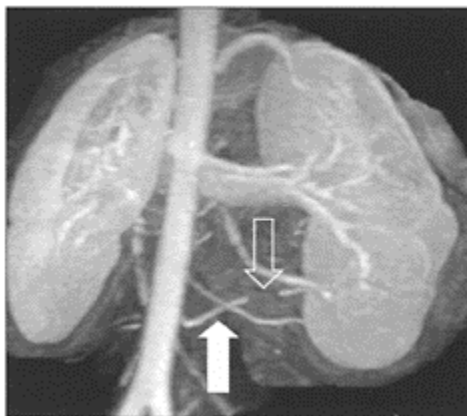
However, there is controversy regarding the import of crossing vessels in regards to success rates of endopyelotomy. A report in 1998 found that 80% of patients had a successful outcome regardless of the presence of a crossing vessel.<sup>83</sup> Questions regarding the additional expense of preoperative imaging (e.g. angiography, spiral CT, or endoluminal US) were raised. However, a later report from the same group 3 years later stated an institutional bias to perform preoperative imaging with spiral CT due to multiple reports of the deleterious effects upon the success rate of endopyelotomy due to crossing vessels.<sup>80</sup>

As regards appropriate imaging for crossing vessels, helical contrast-enhanced CT (HCECT) has replaced conventional intra-arterial digital subtraction angiography (DSA). Rouviere et al, using DSA as a reference standard, found HCECT to be 100% sensitive, and 97% specific for the detection of crossing vessels.<sup>84</sup> Additional information may be obtained from 3D reconstruction of the data obtained during the HCECT, with one study demonstrating 100% concordance between imaging evidence of a crossing vessel and intraoperative findings.<sup>43</sup> Compared to DSA, HCECT provides a relatively noninvasive means of evaluating renal vasculature and its relation to the collecting system. Patients undergoing evaluation with HCECT should first undergo, at the same setting, UECT, to assess for any simultaneous nephrolithiasis. A test injection of contrast (20 ml) may be done with an automated timing system in CT units that are so equipped to allow imaging of the arterial phase at the level of the kidneys during optimal opacification. Alternatively, a rough estimate may be obtained by imaging the aorta at the level of the kidneys every 2–4 s after the test injection to determine the delay from injection to maximal vessel opacification. This is followed by the full contrast injection (120 ml) for

the vascular/arterial phase at a slice thickness of 3 mm and a table speed of 3–6 mm/s (with scanning commencing at the appropriate time after injection). A delayed parenchymal phase may then be obtained at 90–120 s after injection.<sup>13</sup> As with the previously described evaluation of the kidneys with CT, review of the study on a PACS workstation greatly facilitates image interpretation. For those patients with contrast allergy or impaired renal function, MR angiography using intravenously administered gadolinium may be a consideration, with the understanding that resolution of small accessory vessels may be limited (Figures 6.20 and 6.21).<sup>85</sup>



**Figure 6.20** Crossing vessel on MR. Coronal gradient recall gadolinium-enhanced MR images demonstrate an accessory artery supplying the lower pole of the left kidney in a 30-year-old female with symptomatic ureteropelvic junction obstruction. The vessel abuts the lower aspect of the dilated renal pelvis (P).



**Figure 6.21** Crossing vessel on MR 2. 3D reconstructed image from gradient recall gadolinium-enhanced MR images (see Figure 6.20) demonstrate the accessory polar vessel is abutting the ureteropelvic junction (white arrow). Note the drop out in signal due to the overlying dilated renal pelvis, which is not imaged on the GRE pulse sequence (clear arrow).

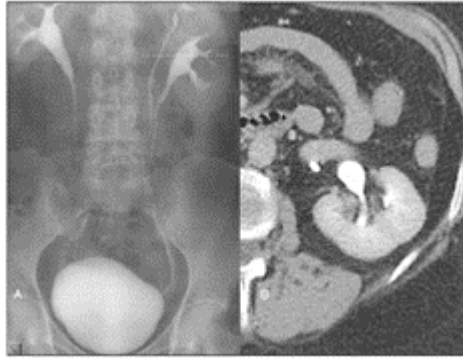
Another modality for consideration in the assessment of crossing vessels is endoluminal ultrasound (EUS), either preoperatively, or at the time of planned endopyelotomy. A 6.2F over-the-wire US probe may be advanced to the level of the UP JO under fluoroscopic guidance after retrograde opacification of the collecting system.<sup>86</sup> Findings of a crossing vessel are suggested by a linear area of hypoechogenicity in close proximity to the center of the transducer sweep. Location of the vessel can be accurately assessed and orientation of the endoluminal incision can be optimally planned. Also, in those situations in which there is a high insertion of the ureter on the pelvis, a septum, representing the ureteral wall against the redundant renal pelvis, may be readily identified and alternative plans made for pyeloplasty. Direct comparison of EUS with helical CT in 20 patients with symptomatic UPJO found that the former modality was more sensitive in the detection of crossing vessels.<sup>87</sup> Crossing vessels were identified in 35% of patients via CT and in 70% by endoluminal US. Thirty-five percent of patients were found by EUS to have a septum, a finding not assessed by CT. Endoluminal US assisted in planning the orientation of endopyelotomy incision in 4 patients and changed the planned operation from endopyelotomy to pyeloplasty in another 4. Thus, almost half of the patients had treatment impacted by EUS findings.



### Imaging in the work-up of the living renal transplant donor

The ultimate goal of laparoscopic renal donation is to expand the pool of potential donors available. Unfortunately, too many patients still die from complications of renal failure while on a waiting list to receive a kidney. With the decreased morbidity of laparoscopic donation, it is hoped that this trend will be ameliorated. Laparoscopic donor nephrectomy has marked advantages over conventional open nephrectomy such as at least a halving of the time of hospital stay and a more rapid return to full activity and employment.<sup>88</sup> Laparoscopic nephrectomy is, however, a challenge to the surgeon due to limitations in exposure, with clear understanding that the safety of the donor is of paramount concern. Essential to the evaluation of the potential laparoscopic renal donor is accurate delineation of the vascular anatomy of the renal allograft. Assessment of renal artery origin, length, branches, and accessory vessels was once obtained with the use of conventional arteriography.<sup>89</sup> Up to one-third of donors have variant renal arterial anatomy. Also to be considered are situations in which the donor has occult vascular disease, such as atherosclerosis or fibromedial disease. Standard IVP was also obtained to evaluate the collecting system for anomalies such as duplications (Figure 6.22). Aberrant anatomy in either case may disqualify a donor, or at the very least may alter the approach at harvest from the donor, or instillation in the recipient.

Conventional arteriography and IVP can now be replaced with helical or multidetector CT, which except for intravenous access for contrast administration, has



**Figure 6.22** Duplication seen on CT-IVP. A 25-year-old female undergoing evaluation as a potential renal donor. (A) IVP demonstrates unsuspected complete duplication of left renal collecting system. (B) CT also demonstrates this duplication. Dashed line in A represents correlation with level of CT image.

become what one investigator has called ‘The marriage of minimally invasive imaging with minimally invasive surgery’.<sup>42</sup> A three-phase protocol is recommended to include a noncontrast evaluation of the kidneys and abdomen at 2.5 mm slice thickness to assess for nephrolithiasis, followed by contrast-enhanced evaluation of the kidneys at 1 mm slice thickness at 25 s and 60 s after contrast administration to assess the arterial anatomy and the parenchyma, respectively (Table 6.4).<sup>42,90</sup> Imaging in the arterial phase should include levels down to the iliac bifurcation to assess for any accessory vessels (Figures 6.23 and 6.24). Venous drainage as regards circumaortic or retroaortic morphology on the left, and adrenal venous anatomy, can also be assessed (Figure 6.25). Three-dimensional images may then be reconstructed on a separate workstation to provide a more familiar product for reference by the surgeon. Finally, a conventional excretory urogram may be obtained several minutes after contrast administration to assess the collecting system, or a topogram may be obtained while the patient remains on the CT table.<sup>90</sup>

Aside from the obviation of the need for invasive arterial access, helical or MDCT evaluation may result in a 50% savings in imaging costs for the prospective renal donor.<sup>91</sup> The accuracy of CT-acquired images in assessing renal arterial anatomy is essentially equal to conventional angiography and superior in assessment of parenchymal and venous anatomy.<sup>92</sup> Because of these advantages, helical CT angiography has been proposed as the initial imaging modality of choice in the evaluation of the potential renal donor.<sup>93</sup>

**Table 6.4** *CT for assessment of renal vasculature*

Position: supine

Scout: AP

Scan area: 2 cm above celiac artery to the bifurcation

Slice increment: 2 mm

Slice thickness: 2 mm

Field of view: varies with patient size

Pitch: 1.5

Rotation time (s): 1

KVP: 120

MA: 225

IV contrast: 125 ml nonionic

Injection rate: 3 ml/s via 20GA angiocath antecubital vein

Scan delay: 25 s after injection or greater, depending on test dose; delayed scans through kidneys to assess parenchyma and veins

Assumes single-detector helical system with pitch=distance couch moves during one revolution of the X-ray tube.



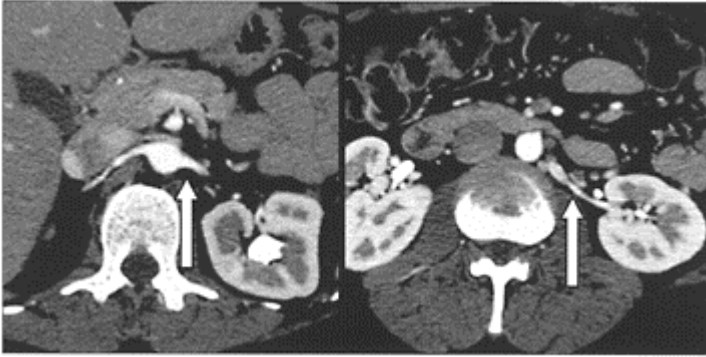
**Figure 6.23** Multiple right renal arteries detected using multidetector CT angiography. A 25-year-old female undergoing evaluation as a potential renal donor. Note extreme detail provided by multidetector technology. Each artery had a separate origin from the aorta.

### Imaging of adrenal lesions

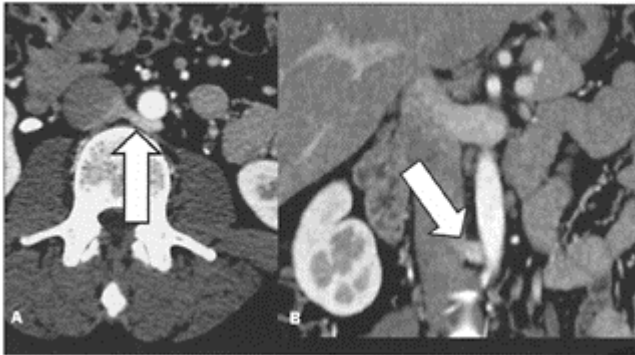
Up to 5% percent of patients undergoing abdominal CT for any indication are found to harbor an adrenal lesion, with the autopsy incidence being up to 8%.<sup>94,95</sup> Despite their small size, the adrenals however are the fourth most common site for metastases from tumors of epithelial origin, with an autopsy incidence of 27%.<sup>96,97</sup> The majority of masses are benign adenomas, even in the setting of known extra-adrenal malignancy. Adenomas tend to be smaller than 3 cm, whereas metastases tend to be multiple and larger. The differential diagnosis of an adrenal lesion includes adenomas, metastases, pheochromocytomas, hemorrhage, myelolipoma, and adrenocortical carcinoma. The role of imaging for the laparoscopic surgeon is to characterize the lesion as benign or potentially malignant, thus providing or refuting a rationale for intervention.

The initial evaluation begins with review of the medical history.<sup>98</sup> Does the patient have hypertension? If so, is the hypertension sustained or episodic? Are aldosterone levels elevated; are serum renin levels low? Is there evidence of hypokalemia? Are there elevations of urinary catecholamines? Such inquiries may help make the diagnosis of Conn's syndrome (due to a functioning adenoma producing aldosterone) or a pheochromocytoma, respectively. Does the patient have a physical examination suggesting hypercortisolism, such as truncal obesity, or hirsutism, seen in Cushing's syndrome from a hyperfunctioning cortisol adenoma? Is there a history of malignancy suggesting metastasis?

In the majority of cases, subsequent CT evaluation can establish a diagnosis. Most adenomas are of low density



**Figure 6.24** Multiple left renal arteries detected using multidetector CT angiography. A 25-year-old female undergoing evaluation as a potential renal donor. Note extreme detail provided by multidetector technology. Each artery had a separate origin from the aorta.



**Figure 6.25** Circumaortic left renal vein detected using multidetector CT angiography. (A) Axial source images. (B) Coronal reconstructed images. A 25-year-old female undergoing evaluation as a potential renal donor.

Normal main left renal vein is seen more cephalad overlying the aorta.  
Note extreme detail provided by multidetector technology.

due to intracytoplasmic lipid. A small well-circumscribed lesion with Hounsfield units on unenhanced CT equal to or less than 10 is of such specificity for the diagnosis of adenoma that no further imaging is felt to be warranted (Figure 6.26).<sup>99</sup> In a meta-analysis of multiple series, Boland et al found that using  $\leq 10$  HU as a demarcation point yielded a sensitivity of 78% and a specificity of 98% for diagnosis of benign adenoma.<sup>100</sup> Such lesions are termed 'lipid-rich' adenomas.

Difficulty arises for those lesions with attenuation values greater than 10 HU. Is the lesion a 'lipid-poor' adenoma or some other entity? Efforts have been made to establish criteria using the contrast washout characteristics of adrenal lesions. A suggested protocol involves directed CT of the adrenal glands at 3–5 mm collimation first unenhanced, repeated 60 s after contrast administration, and finally 15 min later.<sup>101</sup> Identical ROI areas are drawn over the adrenal lesion in question and attenuation values obtained in each phase. Percentage of contrast washout is calculated by the equation:

$$\frac{HU_{\text{enhanced}} - HU_{\text{delayed}}}{HU_{\text{enhanced}} - HU_{\text{unenhanced}}} \times 100\%$$

Well-circumscribed homogenous lesions with contrast washout greater than 60% at 15 min are felt to meet criteria for an adenoma (Fig. 6.27, Table 6.5). Using such a standard and based upon either percutaneous biopsy results or stability over a period of surveillance, Caoili et al were able to correctly characterize 96% of 166 adrenal



**Figure 6.26** Adrenal adenoma on NECT (nonenhanced CT). This 2 cm right adrenal mass was incidentally discovered in a 55-year-old female. The region of interest (ROI) circle was drawn within the lesion, with

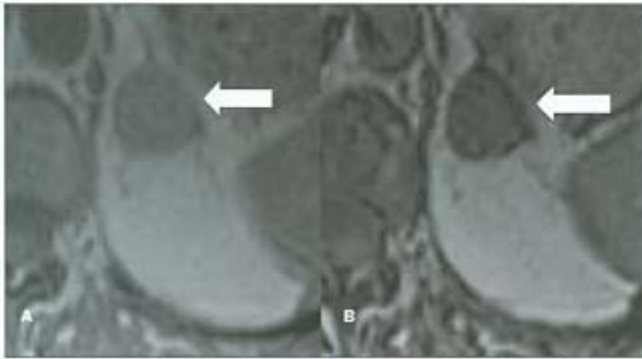
subsequent densitometry yielding a Hounsfield unit of -9.2, indicating a benign adenoma.

masses, yielding a sensitivity and specificity of 98 and 92%, respectively.<sup>101</sup> If there has not been a corresponding unenhanced CT obtained, a relative percent washout equation may be used:

$$\frac{HU_{enhanced} - HU_{delayed}}{HU_{enhanced}} \times 100\%$$

with values greater than 40% suggesting adenoma.<sup>102</sup>

For those patients in whom renal insufficiency or iodinated contrast allergy is a problem, MR may be of benefit. Using T1-weighted GRE techniques there are different reso-



**Figure 6.27** Opposed-phase MR imaging in assessment of possible adrenal adenoma. A 58-year-old female with lung carcinoma found to have left adrenal mass on staging chest CT. Noncontrast CT HU was 25. (A) T1-weighted in-phase axial image demonstrates left adrenal mass (arrow). (B) T1-weighted out-of-phase image demonstrates signal drop out in the left adrenal due to high concentration of intracellular lipid in adrenal cortical tissue. Consistent with benign adenoma.

**Table 6.5** *Adrenal CT protocol*

Position: supine

Scout; AP

Pitch: 0.875

KVP: 120

MA: 300

Rotation time (S): 0.750

Field of view: 300 mm

Scan area: 2 cm above kidneys through bottom of kidneys

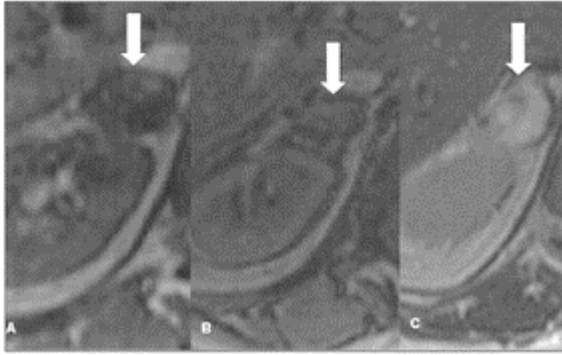
Contrast: nonroutinely used (see below)

Noncontrast scan done first and reviewed by radiologist. If adrenal mass has attenuation <10 HU, no further imaging required (adenoma). If >10 HU, administer IV contrast and time for arterial phase. Delayed images at 15–20 min to evaluate for contrast washout (see text).

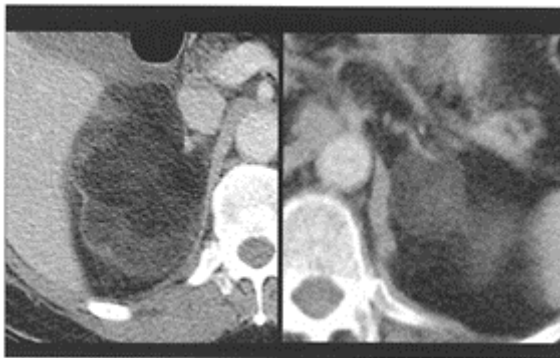
Assumes single-detector helical system with pitch=distance couch moves during one revolution of the X-ray tube.

nant frequency peaks, and thus different signal intensities generated by protons in water molecules of the tissues in nonadenomas vs those in the cytoplasmic triglycerides found in adenomas (Figure 6.28).<sup>103</sup> In initial reports 95% of adenomas were accurately characterized by loss of signal in the adenoma on out-of-phase images (see Figure 6.28). Later reports have reported sensitivities of 81–87% and specificities of 92–100% for accurate characterization of adenomas.<sup>104,105</sup> Gadolinium enhancement or washout has not been found to be of benefit in lesion characterization.” Other lesions of note include pheochromocytomas, myelolipomas, cysts, and carcinomas. Pheochromo-cytomas are usually suggested clinically by episodic hypertension, tachycardia, sweating, and headache. The majority in adults are of adrenal medullary origin, whereas 10% are found to be extra-adrenal and are found near the origin of the inferior mesenteric artery/aortic bifurcation (the organ of Zuckerkandl) or, less commonly, along the sympathetic chain from the thoracic inlet to the pelvis.<sup>106</sup> Evaluation is usually limited to assessment of urinary catecholamines and CT of the abdomen and pelvis. Should CT be non-diagnostic for an adrenal lesion, further evaluation for an extra-adrenal site using I-123 metaiodobenzylguanidine or In-111 octreotide may be of benefit for localization.<sup>95</sup> These adrenal lesions tend to be greater than 3 cm when discovered and tend to be of low signal intensity on T1-weighted MR but are characteristically of high signal intensity on T2-weighted images (Figure 6.29).<sup>97</sup> There may be heterogeneity due to intralesional hemorrhage or necrosis, and there is avid gadolinium enhancement.

Myelolipomas are rare, benign, adrenal lesions containing mature adipose tissues and hematopoietic elements, which, on histologic section, resemble bone marrow (Figure 6.30).<sup>107</sup> The specific finding is that of macroscopic fat, of similar density to the surrounding retroperitoneal fat, easily assessed on noncontrast CT (see Figure 6.30). Density may be variable due to mixed soft tissue density in 20% of cases.<sup>102</sup> Additional hemorrhage or necrosis may complicate imaging diagnosis. While usually an incidental finding, myelolipomas may present with



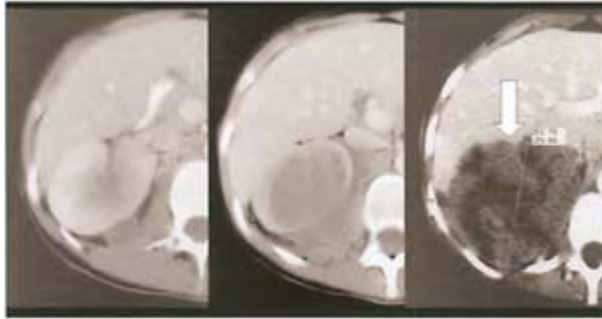
**Figure 6.28** Pheochromocytoma. A 34-year-old female with episodic hypertension and elevated 24-hour urinary catecholamines. (A) Axial T1-weighted in-phase MR image demonstrates left adrenal mass (arrow). (B) Axial T1-weighted out-of-phase MR image demonstrates no significant signal drop out, suggesting lesion is not a benign adenoma. (C) Axial T2-weighted image demonstrates characteristic hyperintensity of pheochromocytoma on T2 imaging.



**Figure 6.29** Adrenal myelolipoma. Representative lesions from two different patients; in each case the lesion was discovered incidentally.

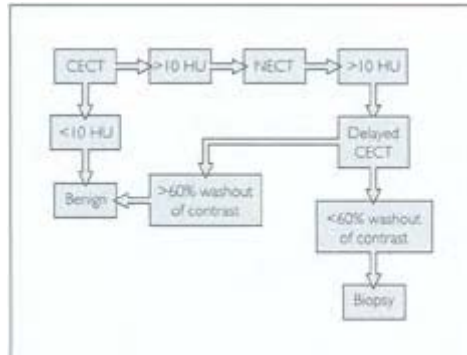


Lesions can attain large size, as seen in image on the left. Note the presence of macroscopic fat in the lesion as compared with the surrounding retroperitoneal fat.



**Figure 6.30** Adrenal cortical carcinoma. CT images of large mass arising near upper pole of right kidney in an 18-year-old female presenting with abdominal pain and stigmata of virilization. The mass involved both the upper pole of the right kidney and the right posterior segment of the liver.

flank pain due to large size, ranging from 2 to 20 cm.<sup>108</sup> On MR, myelolipomas are usually isointense with retroperitoneal fat on T1-weighted images and of intermediate signal intensity on T2-weighted images.<sup>97</sup> Subsequent fatsaturation T1-weighted imaging will demonstrate signal drop out. The differential of such a fatty lesion of the adrenal does include lipoma and liposarcoma, which are comparatively rarer still, although a large lesion may resemble the latter and thus require resection or biopsy even if asymptomatic.



**Figure 6.31** Proposed evaluation of an incidentally discovered solid adrenal lesion. Contrast washout calculated via

$$\frac{HU_{\text{enhanced}} - HU_{\text{delayed}}}{HU_{\text{enhanced}} - HU_{\text{unenhanced}}} \times 100\%$$

CECT=contrast enhanced CT; NECT=nonenhanced CT.

Adrenal cysts may be large, up to 20 cm, when discovered, and exhibit a 3:1 female-to-male predilection.<sup>95</sup> Four types are described: endothelial cysts with possible lymphangiomatous or angiomatous origin; pseudocysts from probable prior hemorrhage; parasitic cysts from echinococcal infection; and, finally, epithelial cysts.<sup>97</sup> Like their renal counterparts, cysts may be further characterized as: uncomplicated, requiring no further evaluation; complicated, requiring resection; and indeterminate, requiring further diagnostic maneuvers, including aspiration, biopsy, or ultimately resection.<sup>108</sup> Enhancement of the wall may merely represent normal adrenal tissue draped over the cyst. While septations may exist, cysts with thicknesses up to 3 mm are allowed to be considered to have benign characteristics.<sup>95</sup> A complicated cyst is defined by a nodular or thick (>5 mm) wall, internal attenuation values greater than 30 HU, and stippled or rim calcifications. Such a cyst should be resected to rule out a cystic adrenal neoplasm.<sup>109</sup>

Adrenal carcinoma is rare (about 2000 cases reported) with approximately 50% of patients manifesting an associated endocrinopathy, usually Cushing's syndrome or a virilizing syndrome in females, feminization in males, or Conn's syndrome.<sup>97,102</sup> Almost 70% of patients present with symptomatic unresectable disease, and usually these patients have large hormonally silent tumors.<sup>110</sup> A solid unilateral adrenal mass larger than 5 cm is considered suggestive of carcinoma and resection of a mass larger than 6 cm is recommended for definitive diagnosis, as surgery provides the only durable treatment (Figure 6.31).<sup>102</sup> Carcinomas tend to be large, with areas of heterogeneity on CT suggesting necrosis; calcification may be seen in 30%.<sup>97</sup> Findings suggesting malignancy include direct involvement of adjacent organs, vena caval invasion and distant metastases. The multiplanar capabilities of MR, and now with MDCT, allow assessment of local invasion, and venous involvement.

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## Anesthetic implications of minimally invasive urologic surgery

Kurt W Grathwohl and Scott Miller

### Introduction

Minimally invasive surgery, specifically laparoscopy, has become increasingly more common because of reduced postoperative pain, shortened convalescence, decreased hospitalization, and significant cost savings.<sup>1-4</sup> The types of laparoscopic procedures and patient indications are also growing as technologies enhance the surgeon's abilities to perform these operations. In fact, the United Kingdom Department of Health predicted that 70–80% of surgical procedures would be performed endoscopically.<sup>5</sup> Consequently, laparoscopy is performed on elderly, pediatric, pregnant, and obese patients as well as those with significant comorbid diseases.

Currently, there are no studies evaluating anesthesiarelated complications of newer minimally invasive laparoscopic surgery, although the incidence is extremely low.<sup>1</sup> Rose and associates in 1992, however, reported anestheticrelated complications of laparoscopic cholecystectomy, noting considerable perioperative morbidity that consisted of hypotension (12.9%), Post-Anesthetic Care Unit hypothermia (31.4%), nausea and vomiting (12.9%), and desaturation (10.9%).<sup>4</sup> More recently, in a 1995 multiinstitutional study of 185 laparoscopic nephrectomy patients, Gill et al reported 1 case of intraoperative pneumothorax which was attributed to transpleural trocar placement.<sup>6</sup> Postoperative anesthetic-related complications included congestive heart failure (3), atrial fibrillation (2), myocardial infarction (1), pneumonitis (2), pulmonary embolism (1), brachial nerve palsy (1), lateral compartment syndrome (1), non-oliguric acute tubular necrosis (1), and confusion (1).<sup>6</sup> Kavoussi and associates evaluated 372 laparoscopic pelvic lymph node dissection patients at eight medical centers in 1993 and found anesthesia-related complications in 9 cases (2.4%): hypercarbia (1), prolonged sedation (1), obturator nerve palsy (2), and lower extremity deep venous thrombosis (5).<sup>7</sup> There were no deaths in either study.<sup>6,7</sup> The incidence of complications also varies widely, depending on the type of procedure and the experience of the surgeon.<sup>1</sup>

Despite improved outcomes and the minimally invasive title, laparoscopy can be associated with major cardiopulmonary perturbations and anesthesia-related complications (Table 7.1) that pose significant challenges to the anesthetist and surgical team. Subsequently, laparoscopy



**Table 7.1** *Anesthetic-related complications of laparoscopic surgery*

***Intraoperative***

Gastroesophageal reflux/aspiration pneumonitis  
Positioning-related nerve injury  
Positioning-related physiologic effects  
Hemorrhage from vascular injury  
Fluid therapy overload  
Hypothermia

***Associated with insufflation/pneumoperitoneum***

Vagal response  
Cardiac arrhythmias  
Hypercarbia  
CO<sub>2</sub>/gas embolism  
Emphysema (subcutaneous, preperitoneal)  
Pneumothorax/pneumomediastinum/ pneumopericardium  
Hypotension  
Hypertension  
Elevated peak airway pressures  
Hypoxemia  
Oliguria

***Postoperative***

Nausea/emesis  
Abdominal/shoulder pain  
Pulmonary impairment

mandates a vigilant knowledgeable anesthetist and communication with the entire surgical team.

The primary anesthetic goals for minimally invasive surgery include:

1. patient safety
2. avoidance or early treatment of pathophysiologic changes associated with laparoscopy
3. amnesia/analgesia
4. ideal surgical field, i.e. muscle relaxation, position, etc.
5. rapid recovery
6. therapy for adverse effects of anesthesia, i.e. nausea/ vomiting.

The aim of this chapter is to review, enhance, and facilitate the anesthetist and surgeon's appreciation of the unique anesthetic-related implications of minimally invasive urologic surgery to improve communication and patient safety.

### **Physiologic considerations unique to laparoscopy**

Pneumoperitoneum after peritoneal insufflation and alterations in patient position causes several physiologic effects unique to laparoscopy. Hemodynamic changes during brief procedures in healthy patients are minimal; however, patients with preoperative cardiopulmonary disease demonstrate significant pathophysiologic changes.<sup>8-10</sup>

Relatively high solubility and lack of combustion make CO<sub>2</sub> the most common gas utilized for peritoneal insufflation, although N<sub>2</sub>O or He can be used.<sup>11,12</sup> Carbon dioxide is also highly permeable, approximately 20 times that of O<sub>2</sub>. Peritoneal insufflation pressures of 10–25 mmHg plus 100% CO<sub>2</sub> at atmospheric pressure (760 mmHg) creates a large gradient for CO<sub>2</sub> diffusion into the bloodstream (CO<sub>2</sub> partial pressure 40 mmHg). Most of the transperitoneally absorbed CO<sub>2</sub> is converted to bicarbonate for transportation in the blood until the oxidation of hemoglobin causes CO<sub>2</sub> to be released in the alveolar capillaries and expired. Absorption of CO<sub>2</sub> causes an increased arterial pressure of CO<sub>2</sub> (PaCO<sub>2</sub>). This is easy to understand, since PaCO<sub>2</sub> is directly related to CO<sub>2</sub> production (VCO<sub>2</sub>)—sum of metabolic CO<sub>2</sub> and adsorbed CO<sub>2</sub>—and inversely related to alveolar ventilation (VA) by the equation:

$$\text{PaCO}_2 = 0.863(\text{VCO}_2)/\text{VA}.$$

Furthermore, alveolar ventilation is determined by total minute ventilation (VE) minus dead space ventilation (VD):

$$\text{VA} = \text{VE} - \text{VD}.$$

The net effect, therefore, without a change in alveolar ventilation is an increase in PaCO<sub>2</sub>. The elevation of PaCO<sub>2</sub> is unpredictable in patients with cardiopulmonary disease, but an average increase in PaCO<sub>2</sub> among 3 studies comparing laparoscopy of less than 30 min was 10.7 mmHg.<sup>2,8,9</sup> Consequently, patients also typically demonstrate mild respiratory acidosis.<sup>2,8,9</sup>

Carbon dioxide acts directly to inhibit the cardiovascular system, decreasing heart rate, cardiac contractility, and systemic vascular resistance (SVR) while increasing pulmonary artery pressures.<sup>1,5,13,14</sup> Stimulation of sympathetic nervous system efferents and increased circulating catecholamines from the adrenal medulla caused by CO<sub>2</sub>, however, result in increased heart rate, contractility, and SVR, with net increases in cardiac output (CO) and blood pressure.<sup>2,5,10</sup> Cardiac arrhythmias are also frequently seen with hypercarbia.<sup>2,13</sup> There are several mechanical effects of increased intraabdominal pressure (IAP) from pneumoperitoneum.

Compression of the abdominal aorta contributes to an increased SVR and afterload, which can result in decreased CO.<sup>5,10</sup> Venous compression, likewise, results in decreased CO secondary to an initial increased venous return to the heart followed by a significant decline in inferior vena cava flow and reduced cardiac preload.<sup>15</sup> Cephalad shift of the diaphragm increases intrathoracic pressures, resulting in elevated central venous pressures. Heart rate is also increased by IAP independent of CO<sub>2</sub>.<sup>2</sup> Cephalad elevation of the diaphragm by IAP also results in several pulmonary effects including decreased functional residual capacity (FRC) and respiratory compliance, as well as increased pulmonary dead space, shunt, and peak airway pressure.<sup>8,10,16</sup> These effects are magnified or may be altered with the administration of anesthetic, in obese patients, lateral decubitus, and Trendelenburg positions, although the contribution of position is now debated.<sup>2,16–18</sup> The effects of position may be attenuated by peritoneal insufflation in the supine position prior to movement into Trendelenburg or reverse Trendelenburg positions.<sup>16–18</sup> As a consequence of these combined cardiopulmonary changes, oxygenation may worsen, although it is typically easily increased by raising the inspired O<sub>2</sub> concentration.<sup>12,17,19</sup> Table 7.2 summarizes the cardiopulmonary effects of IAP,

although alterations are dependent on several patient and surgical interactions such as the chosen anesthetic, preoperative fluid balance, position, degree of IAP, type and duration of the procedure, etc. Furthermore, patients with underlying cardiopulmonary diseases may display accentuated responses to the laparoscopic-induced physiologic changes.<sup>2,8</sup>

Increased IAP and resultant cardiovascular changes also cause several regional circulatory and endocrine aberrations. Elevated CO<sub>2</sub> and IAP increase cerebral blood flow and intracranial pressure (ICP), although the clinical significance is not clear.<sup>5,20</sup> Splanchnic perfusion and hepatic blood flow are decreased, resulting in gastric mucosal hypoperfusion.<sup>5</sup> Both neurohumoral factors, such

**Table 7.2** *Cardiopulmonary responses to pneumoperitoneum 25 mmHg*

|   |    |
|---|----|
| Heart rate                              | ↑↔ |
| Stroke volume                           | ↓  |
| Mean arterial pressure                  | ↑  |
| Systemic vascular resistance            | ↑  |
| Cardiac output                          | ↓  |
| Central venous pressure                 | ↑  |
| Functional residual capacity            | ↓  |
| Respiratory compliance                  | ↓  |
| Peak airway pressures                   | ↑  |
| PaO <sub>2</sub>                        | ↓↔ |
| PaCO <sub>2</sub>                       | ↑  |
| pH                                      | ↓↔ |
| ↑, increases; ↓ decreases; ↔ no change. |    |

as increased antidiuretic hormone (ADH or vasopressin), and mechanical compression of the renal arteries and veins decrease renal blood flow, glomerular filtration rate (GFR), sodium excretion, and creatinine clearance.<sup>5,15</sup> Finally, decreased lower limb venous flow has been speculated to increase risk of deep venous thrombosis (DVT), although data are confounding.<sup>5,7</sup>

Helium peritoneal insufflation has been used to prevent the adverse physiologic sequelae of hypercarbia in patients with severe pulmonary disease and pheochromocytoma.<sup>11,12</sup> The lower solubility of helium, however, may theoretically worsen the outcome of venous gas embolism, which limits its use.<sup>12</sup>

**Preoperative preparation**

The potentially severe cardiopulmonary changes associated with minimally invasive surgery make it imperative that a thorough pre-anesthetic assessment is performed on every patient. Even though laparoscopy is not contraindicated in obesity, extremes of age, pregnancy, and those with severe cardiopulmonary disease, it is important to insure that the patient is medically maximized in order to safely tolerate the physiologic changes. Moreover, the potential for conversion to an open procedure necessitates that the patient

be counseled appropriately and is medically ready to tolerate the surgical stress associated with these procedures. Standards for preoperative assessment have been outlined and should be adhered to.<sup>21,22</sup>

The preoperative evaluation also allows the anesthetist to properly plan perioperative management and it serves to decrease patient anxiety. In one study, information obtained during the pre-anesthetic evaluation resulted in changes of care plans in 20% of all patients.<sup>23</sup> For instance, a patient may be found to have severe pulmonary disease or pulmonary hypertension that may require the avoidance of CO<sub>2</sub> insufflation.<sup>12</sup>

Practice guidelines for preoperative fasting and the use of pharmacologic agents to reduce the risk of pulmonary aspiration have been published and, as with all surgical procedures, should be adhered to.<sup>24</sup>

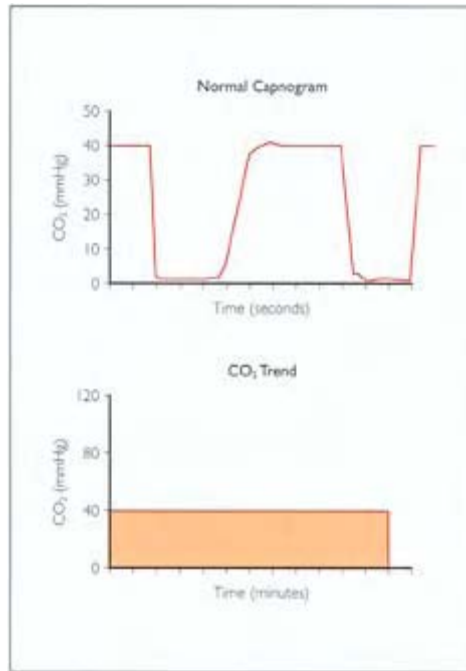
The perioperative evaluation and management of patients with pheochromocytoma is well known and should not be different for laparoscopic adrenalectomy of pheochromocytoma. Increased release of catecholamines during anesthesia and tumor manipulation may exacerbate the pathophysiologic effects of CO<sub>2</sub>-induced pneumoperitoneum, although reports have been conflicting.<sup>11,12,25–27</sup>

### *Monitoring considerations*

Routine intraoperative monitoring should include electro-cardiogram, noninvasive blood pressure, temperature sensor, concentration of oxygen in the patient's breathing system, pulse oximetry, and capnography. Mechanically ventilated patients should also have tidal volume and airway pressure monitoring. Urinary output is measured after bladder catheterization, which also serves to decompress the bladder prior to trocar placement.

Continuous capnography is useful in monitoring the effects of CO<sub>2</sub> absorption and the adverse cardiopulmonary effects of laparoscopy and anesthesia. Capnography measures exhaled CO<sub>2</sub> breath by breath, allowing for determination of end-tidal CO<sub>2</sub> (ETCO<sub>2</sub>). Figure 7.1 shows a normal capnogram. Under normal physiologic conditions in healthy patients ETCO<sub>2</sub> approximates PaCO<sub>2</sub>. A small gradient (PaCO<sub>2</sub>—ETCO<sub>2</sub>) of approximately 5 mmHg exists because of dilution by dead space gases. End-tidal CO<sub>2</sub> is normally maintained between 35 and 40 mmHg to ensure PaCO<sub>2</sub> less than 45 mmHg. However, increased dead space ventilation in chronic obstructive pulmonary disease, acute respiratory distress syndrome, and acute decreases in cardiac output, etc., increases PaCO<sub>2</sub>—ETCO<sub>2</sub> and makes ETCO<sub>2</sub> unreliable as an estimate of PaCO<sub>2</sub> in these circumstances.<sup>8,28</sup> Arterial blood gas sampling therefore remains the gold standard for evaluation of unanticipated trends or changes.<sup>8</sup>

Arterial line placement for blood gas analysis allows close monitoring in prolonged procedures and in patients with severe cardiopulmonary diseases. Central venous pressure (CVP), pulmonary artery catheter (PAC) monitoring and transesophageal echocardiography (TEE) are also indicated in patients with severe cardiopulmonary diseases and pheochromocytoma.<sup>26,29</sup> Portera et al prospectively evaluated 10 cardiac patients and found that the PAC identified 2 patients who developed postoperative



**Figure 7.1** Normal capnogram. CO<sub>2</sub> reaches near 0 at the end of inspiration and beginning of expiration when dead space gas is exhaled. As expiration continues, CO<sub>2</sub> rises rapidly toward the alveolar plateau, which lasts for the greater part of the trace. ETCO<sub>2</sub> is measured immediately before inspiration begins the rapid downslope.

congestive heart failure.<sup>29</sup> Interpretation of CVP and PAC may be problematic, however, because IAP increases intrathoracic pressures, artificially elevating CVP, and pulmonary artery occlusion pressures.<sup>28</sup> Transesophageal echocardiography is useful for the evaluation of left ventricle regional wall motion abnormalities while continuous monitoring for the identification of gas embolism is not clinically practical. One recent study utilizing TEE identified unexpected increased regurgitant valvular lesions in 15 of 16 healthy laparoscopic donor nephrectomy patients, although the significance is not clear.<sup>30</sup>

### *Anesthetic techniques*

General anesthesia is most commonly chosen for transretroperitoneal or retroperitoneal laparoscopic procedures because of positioning requirements, need for optimal muscle relaxation, time to accomplish the procedure, patient discomfort associated with pneumoperitoneum, and the need to control ventilation in patients with cardiopulmonary diseases. Regional and even local anesthesia, however, is increasingly performed in nonurologic laparoscopy.<sup>31,32</sup> Advantages of regional techniques (subarachnoid, epidural block) includes less postoperative pain and decreased emesis.<sup>31,32</sup> Additionally, Chiu et al studied the cardiopulmonary effects of laparoscopic ligation of bilateral spermatic varices under epidural anesthesia and found decreased physiologic perturbations.<sup>33</sup> Further evaluation is necessary before this can be recommended for patients with severe comorbid conditions. Disadvantages of regional techniques include the requirement for a T4 block to allow adequate analgesia, which is associated with dyspnea and sympathetic blockademediated hypotension.<sup>2,32</sup> Subdiaphragmatic irritation from the insufflated gas also results in shoulder pain despite the high level of blockade.<sup>32</sup> Hyperbaric subarachnoid block may cause severe sympathectomy and hypotension when utilized in the Trendelenburg position and should be avoided while the risk with hypobaric solutions is reduced.<sup>2,31,32</sup>

General anesthesia and muscle relaxation afford the anesthetist and surgeon optimum conditions. Aspiration from positioning and peritoneal insufflation is reduced with cuffed endotracheal tube placement, although the laryngeal mask airway (LMA), which does not protect gastric content aspiration, has been utilized in shorter procedures.<sup>3,32</sup> Oro/nasogastric decompression after anesthetic induction further decreases aspiration risk and facilitates safe trocar placement.<sup>33</sup> Chiu and Ng reported two cases of gastric perforation secondary to trocar placement associated with gastric insufflation during anesthesia induction.<sup>34</sup> Mechanical ventilation allows adjustment of  $\text{ETCO}_2 < 45 \text{ mmHg}$ . There are no clear differences in anesthetic agents, although DeGrood et al discovered that patients who received total intravenous anesthesia with propofol compared to isoflurane experienced less nausea and faster postoperative recovery.<sup>35</sup>

Nitrous oxide ( $\text{N}_2\text{O}$ ) has several properties that make it a useful anesthetic. While not potent enough to be utilized alone, it decreases the minimum alveolar concentration (MAC) of the volatile anesthetic agents and its low solubility creates rapid induction and emergence. Nitrous oxide stimulates the sympathetic nervous system, which may exacerbate and confound the effects of peritoneal insufflation. Furthermore,  $\text{N}_2\text{O}$  is 35 times more soluble than nitrogen, which can produce bowel distention as well as worsen the effects of air embolism and pneumothorax.<sup>36</sup> During short procedures, there is little consequence; however, procedures lasting  $>2\text{--}4$  hours can cause significant bowel distention of over 100–200%.<sup>36</sup> Desflurane, a newer volatile anesthetic agent, obviates the need for  $\text{N}_2\text{O}$  since it has a blood-gas partition coefficient less than  $\text{N}_2\text{O}$ , resulting in very rapid induction and emergence when used as the sole anesthetic. Interestingly, despite these concerns, almost all of the reports we reviewed regarding laparoscopic surgery included  $\text{N}_2\text{O}$  as part of the anesthetic regimen.

## **Anesthetic-related complications**

### *Intraoperative*

#### **Gastroesophageal reflux/aspiration pneumonitis**

Several diseases such as diabetic gastropathy, hiatal hernia, and renal failure, as well as Trendelenburg position and IAP from peritoneal insufflation, theoretically predispose patients to an increased risk of aspiration during anesthesia. However, controversy currently exists regarding the effects of IAP.<sup>3,37</sup> One study found that increased IAP raised lower esophageal sphincter pressure to a greater degree than intragastric pressure, thereby actually decreasing the risk of regurgitation.<sup>37</sup> Additionally, studies evaluating the risk of aspiration utilizing the LMA during gynecologic laparoscopy failed to document clinically significant aspiration or reflux.<sup>38</sup> Realistically, the risk for laparoscopic procedures is probably not different from other intra-abdominal surgical procedure. Needless to say, the aspiration risk is significantly decreased after intubation with a cuffed endotracheal tube and when preoperative fasting guidelines are followed.<sup>24</sup> Oro/nasogastric decompression after intubation may further decrease the risk of large-volume gastric content aspiration. Clinically, intraoperative findings of significant aspiration include hypoxemia, elevated peak airway pressures from bronchospasm, and, potentially, hypotension (see Tables 7.5, 7.7, and 7.8).

#### **Positioning-related nerve injury**

Care must be taken to avoid direct mechanical compression or excessive stretch on nerves. While the ulnar nerve is the most frequently injured nerve associated with anesthesia, the pathophysiologic mechanism remains elusive.<sup>39</sup> The lithotomy position has been associated with compression and resultant common peroneal nerve injury.<sup>40</sup>

#### **Positioning-related physiologic effects**

Position-related pulmonary and cardiovascular changes are common in lateral decubitus, and head up or down positions. Head-down position increases central venous pressure and CO. Usually, these changes are of minimal clinical significance, although patients with significant coronary artery disease may not tolerate increases in myocardial oxygen demand. As mentioned previously, pneumoperitoneum decreases FRC and pulmonary compliance, resulting in ventilation/perfusion (V/Q) mismatch and predisposing the patient to hypoxemia. Obese patients or those with coexisting respiratory disease exhibit marked responses that are magnified with increased head-down position. Pneumoperitoneum and the head-down position exacerbates raised ICP seen in patients with head trauma.<sup>5</sup> The head-up position and pneumoperitoneum usually results in a decrease in CO from a fall in preload,<sup>5,41</sup> while respiratory perturbations observed from pneumoperitoneum improve. Pneumatic compression stockings may attenuate impaired venous return by improving lower extremity venous blood flow.<sup>42</sup>

### **Hemorrhage from vascular injury**

Fortunately, significant morbidity and mortality from vascular injury is rare, as is re-exploration from post-operative hemorrhage. Most injuries result from trocar or Veress needle insertion. However, as increasingly complex laparoscopic surgeries are being performed, requiring multiple ports, the risk of abdominal wall vessel injuries are becoming more common.<sup>1</sup> In some instances, particularly if an abdominal wall vessel or retroperitoneal vessel are injured, the bleeding can be concealed. One must have a high degree of suspicion for hemorrhage if the patient develops hypotension or has a falling hematocrit. In patients who have involved laparoscopic procedures or known bleeding diathesis, type and screen should be performed.

### **Fluid therapy overload**

The hemodynamic effects of laparoscopy may be magnified by hypovolemia, necessitating adequate intravascular volume replacement; however, several cases of presumed volume overload have been reported during laparoscopic procedures.<sup>6</sup> One author suggests limiting intravenous fluid therapy rates to 3–5 ml/kg/h.<sup>2</sup> Insensible fluid losses and interstitial space requirements are significantly less during laparoscopic procedures compared to open laparotomy or retroperitoneal procedures, where fluid losses can exceed 8–12 ml/kg/h.<sup>6</sup> The oliguric state secondary to vena cava and renal vein compression also creates the impression of decreased intravascular volume, which may lead to overhydration.<sup>43,44</sup> Clinical findings associated with fluid therapy volume overload include hypertension and hypoxemia from pulmonary edema. Cardiac patients may also develop myocardial ischemia and congestive heart failure manifested by arrhythmias, oliguria, and hypotension.

### *Associated with insufflation/pneumoperitoneum*

#### **Vagal response**

Insertion of the Veress needle or trocar, but more commonly peritoneal stretching from gas insufflation, can cause a profound vagal response manifested by hypotension, bradycardia, atrioventricular dissociation, and even asystole.<sup>1,9,32</sup> Correction is usually easily achieved by cessation of the surgical stimulation, release of the pneumoperitoneum, and the administration of atropine.<sup>1,9,19,32</sup>

#### **Cardiac dysrhythmias**

As mentioned earlier, the heart rate either does not change or slightly increases during insufflation and pneumoperitoneum. Bradydysrhythmias are common during insufflation.<sup>1</sup> Tachydysrhythmias occur less often but are common in the setting of hypercarbia, hypoxemia, acidosis, inadequate levels of anesthesia, and embolic events.



**Hypercarbia**

Hypercarbia is typically diagnosed intraoperatively when the ETCO<sub>2</sub> rises > 45 mmHg. While it is well known that the insufflation of CO<sub>2</sub> results in the elevation of PaCO<sub>2</sub> and its adverse physiologic consequences (see Physiologic considerations unique to laparoscopy section above), there are several other diagnostic considerations.<sup>13</sup> Hypercarbia typically occurs over the first 10 min of insufflation. Given the equation

$$\text{PaCO}_2 = 0.863 (\text{VCO}_2) / \text{VA}$$

where

$$\text{VCO}_2 = \text{metabolic CO}_2 + \text{absorbed CO}_2$$

and

$$\text{VA} = \text{VE} - \text{VD}$$

elevations of PaCO<sub>2</sub> can arise from only four sources:

- 1. increased metabolic production of CO<sub>2</sub>
- 2. increased absorbed CO<sub>2</sub>

**Table 7.3** *Differential diagnosis of elevated PaCO<sub>2</sub> During general anesthesia with mechanical ventilation*

|   | Effect on<br>ETCO <sub>2</sub> |
|---|--------------------------------|
| <b><i>Increased metabolic production</i></b>  |                                |
| Pyrexia   | ↑                              |
| Sepsis  | ↑                              |
| Malignant hyperthermia  | ↑                              |
| Shivering   | ↑                              |
| Thyroid storm   | ↑                              |
| Catecholamine release/pheochromocytoma  | ↑                              |
| <b><i>Increased CO<sub>2</sub> absorption</i></b>   |                                |
| CO <sub>2</sub> -induced pneumoperitoneum   | ↑                              |
| CO <sub>2</sub> -induced subcutaneous emphysema/pneumomediastinum                             | ↑                              |
| Capnotherax   | ↑                              |
| CO <sub>2</sub> rebreathing from failure of CO <sub>2</sub> absorber/breathing circuit valves | ↑                              |
| <b><i>Decreased alveolar ventilation</i></b>  |                                |
| Mechanical failure of endotracheal tube, breathing circuit, or ventilator                     | ↑                              |
| <b><i>Increased dead space ventilation</i></b>  |                                |
| Pulmonary thromboembolism   | ↓                              |
| Pulmonary gas embolism  | ↓                              |
| Increased positive end-expiratory pressure (PEEP)   | ↓                              |
| High peak/plateau airway pressure   | ↓                              |

Pulmonary disease

↓↑

Hypotension

↓

↑, increased; ↓ decreased. Increased dead space ventilation causes V/Q mismatch, which will increase the  $\text{PaCO}_2$ — $\text{ETCO}_2$  gradient. Increased PEEP and high airway pressures distend normal alveoli and compress alveolar capillaries, increasing dead space ventilation. Pulmonary diseases such as bronchospasm, asthma, and chronic obstructive pulmonary disease may demonstrate elevations in  $\text{ETCO}_2$  when  $\text{PaCO}_2$  is dramatically elevated.

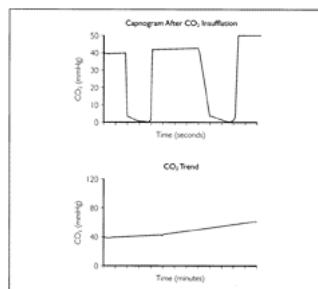
3. decreased alveolar ventilation or

4. increased dead space ventilation.

See Table 7.3 for the differential diagnosis of elevated  $\text{PaCO}_2$  during general anesthesia with mechanical ventilation. Figure 7.2 demonstrates the gradual increase in  $\text{ETCO}_2$  seen in these cases with the exception of increased dead space ventilation.

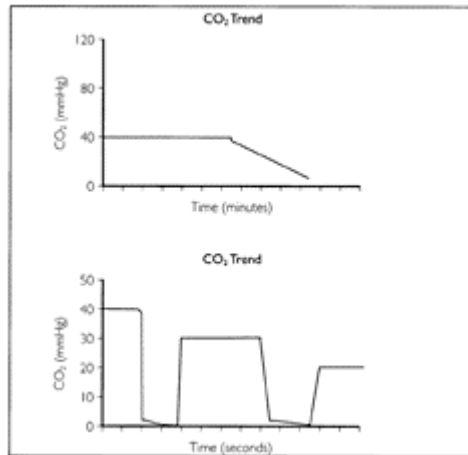
The  $\text{ETCO}_2$  is a reliable intraoperative indicator of hypercarbia in healthy patients, although it may be unreliable in patients with cardiopulmonary disease secondary to V/Q mismatching from increased dead space ventilation.<sup>1,8,28</sup> Likewise, any cause of increased  $\text{PaCO}_2$  from dead space ventilation will also cause an increased  $\text{PaCO}_2$ — $\text{ETCO}_2$  gradient as a result of a concomitant decrease in  $\text{ETCO}_2$ . As a matter of fact, the  $\text{ETCO}_2$  may dramatically decrease during pulmonary gas embolism, hypotension, etc. (Figure 7.3), despite significantly elevated  $\text{PaCO}_2$ , making capnometry a valuable diagnostic tool and monitor in laparoscopy. Arterial blood gas analysis, however, still remains the gold standard for evaluation of  $\text{PaCO}_2$ .<sup>8</sup>

In mechanically ventilated healthy patients the elevation of  $\text{ETCO}_2$  and  $\text{PaCO}_2$  is easily remedied by increasing alveolar ventilation through increased respiratory rate or secondly tidal volumes.<sup>2</sup> In rare circumstances or in patients with severe cardiopulmonary disease, increased ventilation may be prohibited or ineffective, necessitating conversion to an open procedure.<sup>2</sup> Wittgen and associates reported 10 patients for laparoscopic cholecystectomy with cardiac or pulmonary disease and recorded one case of conversion to an open procedure for severely elevated



**Figure 7.2** Capnogram after  $\text{CO}_2$  insufflation. Capnometry demonstrating the slow increase in  $\text{CO}_2$  seen with  $\text{CO}_2$  absorption and other causes of increased  $\text{CO}_2$

production or decreased alveolar ventilation.



**Figure 7.3** Capnogram with increased dead space ventilation. Capnometry demonstrating a decrease in  $\text{ETCO}_2$  seen in cases of increasing dead space ventilation such as pulmonary embolism or decreased cardiac output. Bronchospasm, asthma, and chronic obstructive diseases demonstrate a characteristic upslope of the expired  $\text{CO}_2$  without a plateau or identifiable end tidal point.

$\text{PaCO}_2$  and acidosis.<sup>8</sup> Table 7.4 lists the diagnostic and therapeutic maneuvers that should be performed when faced with severely increased  $\text{ETCO}_2$ . Life-threatening complications should be ruled out or treated before a diagnosis of  $\text{CO}_2$  absorption is made. A decreasing  $\text{ETCO}_2$  particularly in the face of unchanged ventilation, hypotension or oxygen desaturation should also prompt thorough diagnostic and therapeutic maneuvers to rule out pulmonary gas embolism or thromboembolism.

Carbon dioxide may be stored in tissues remaining persistently elevated even after desufflation.<sup>2</sup> Patients should therefore be monitored prior to and after extubation to ensure adequate minute ventilation.<sup>2</sup>

### **$\text{CO}_2$ /gas embolism**

Carbon dioxide embolism to the heart or pulmonary vessels has been observed in 69% of patients during laparoscopic cholecystectomy.<sup>45</sup> Fahy postulated, as have others, that gas embolism would be higher in laparoscopic nephrectomy because of associated renal vein manipulation.<sup>1,30</sup> Fahy's study, utilizing continuous TEE, documented only one episode of gas embolism, out of 16 cases (6%) which did not result in any hemodynamic instability.<sup>30</sup> The

**Table 7.4** *Evaluation and management of elevated ETCO<sub>2</sub> during mechanical ventilation*

| Evaluation  | Therapy  |
|---|--|
| 1. Ensure adequate oxygenation  | 1. Place on 100% FiO <sub>2</sub>  |
| 2. Auscultate for bilateral breath sounds; R/O mechanical malfunction<br>capnotherax/endobronchial intubation<br>wheezing | 2. Use alternative breathing circuit, decompress chest, reposition ETT, treat bronchospasm<br>3. Change CO <sub>2</sub> absorber, inspiratory and expiratory valves, increase fresh gas flow |
| 3. Check inspired CO <sub>2</sub> level, >2 mmHg indicates rebreathing  | 4. Increase alveolar ventilation: tidal volumes 10–12 ml/kg or PAWP <35 respiratory rate maximum 18–24 avoid PEEP if O <sub>2</sub> adequate insure adequate intravascular volume            |
| 4. Associated with CO <sub>2</sub> insufflation   |  |
| 5. Check arterial blood gas; R/O causes of increased CO <sub>2</sub> production: pyrexia, malignant hyperthermia, etc.    | 5. As indicated; cooling, dantrolene   |
| 6. Palpate skin to R/O subcutaneous CO <sub>2</sub> emphysema   | 6. Create 'blow holes' to allow CO <sub>2</sub> escape<br>7. Limit intra-abdominal pressure, change patient position   |
| 7. Other etiologies excluded PaCO <sub>2</sub> >55 mmHg with acidosis   | 8. Convert to an open procedure  |
| 8. Associated with hypotension, hypoxemia or severe elevations in PAWP  |  |

FiO<sub>2</sub>, fractional inspired concentration of oxygen; R/O, rule out; ETT, endotracheal tube; PAWP, peak airway pressure; PEEP, positive end-expiratory pressure.

This is a suggested algorithm that can be followed to evaluate and treat severe increases in ETCO<sub>2</sub>. The therapies are not intended to be mutually exclusive. Endobronchial intubation would be an uncommon cause of elevated CO<sub>2</sub> but can be seen in patients with cardiopulmonary diseases.

exact incidence of gas embolism is not known but it remains rare.<sup>45,46</sup> Unfortunately, gas embolism can be catastrophic resulting in severe cardiovascular collapse or death.<sup>1,19,45,46</sup>

During laparoscopy, initial insufflation of pressurized gas is the most common period to observe gas embolism.<sup>2,45</sup> Vascular injury or direct placement of the Veress needle/trocar into a vein or a highly vascularized parenchymal organ such as the liver can cause significant embolism if not detected early.<sup>1,2,46,47</sup> The high solubility of CO<sub>2</sub> means that significantly larger volumes of gas (>25 ml/kg, 1200 ml, >1 liter/min) are necessary compared to air (>3–5 ml/kg, 240 ml), He, etc., to cause clinically significant embolism.<sup>1,2,48</sup> If an embolism does occur, its solubility results in rapid resolution.<sup>1,46</sup> The risk of embolism is decreased by mechanical ventilation with positive pressure, adequate hydration, limiting CO<sub>2</sub> insufflation pressure and volume to less than 30 mmHg and 3 liters.<sup>45,46</sup> Monitoring with precordial Doppler and TEE has been advocated for

procedures with significant risk such as posterior fossa craniotomy in the sitting position but is not practical on a routine basis for laparoscopy.

Clinical signs include sudden hypotension, hypoxemia, tachycardia, and arrhythmias.<sup>45,46</sup> End-tidal CO<sub>2</sub> may initially increase, but if the embolism does not resolve quickly, it will fall dramatically (see Figure 7.3) from cardiovascular collapse and decreased pulmonary perfusion. The classical finding of a 'mill wheel murmur' is a late finding that is rarely appreciated in air embolism but has been appreciated in CO<sub>2</sub> embolism.<sup>46</sup> Therapy includes immediate cessation of pressurized gas, discontinuation of N<sub>2</sub>O, administration of 100% O<sub>2</sub>, Valsalva maneuver to prevent further gas entry into the heart and lungs, elevation of CVP by administration of intravenous (IV) fluids, and hemodynamic/cardiac support as needed. Nitrous oxide has been traditionally thought to not increase the size of CO<sub>2</sub> bubbles because of similar solubilities, but Junghans demonstrated in a recent study that the addition of N<sub>2</sub>O did in fact worsen hemodynamics and cardiac function.<sup>49</sup> The optimum patient position to limit and treat gas embolism is currently controversial. Most authors recommend the position described by Durant over 50 years ago—Trendelenburg (head down), left lateral decubitus to trap air in the right ventricle—although recent animal studies do not support this.<sup>50–52</sup> Blood flow rather than buoyancy of the bubble determined the course of air emboli in one animal study.<sup>50</sup> Geissler et al studied venous air embolism with TEE, and found that body position did not benefit hemodynamic performance and that cardiac decompensation was not from air lock of the right ventricular outflow tract but rather the effects of right ventricular ischemia.<sup>52</sup> Trendelenburg position may also exacerbate the resultant cerebral edema, pulmonary mechanics, and hemodynamics seen with cephalad movement of the diaphragm.<sup>46,52</sup> Practically speaking, the supine position facilitates therapeutic intervention, i.e. central venous access, cardiopulmonary resuscitation (CPR), etc., although further studies are needed to establish the optimum position for resuscitation. Clinically, placement of a central line if not already in situ, with aspiration of air, may take several minutes, and hyperbaric therapy, while controversial, may also not be readily available.<sup>2</sup> If cardiac arrest occurs and embolism does not correct quickly, thoracotomy with direct aspiration, internal cardiac massage, and cardiac bypass may be life saving. Up to 20% of adults have a probe patent foramen ovale which may result in right-to-left embolism and cerebral infarction.<sup>2</sup> Also, it is debatable if, like air, CO<sub>2</sub> initiates the release of inflammatory mediators, resulting in vascular endothelial damage and causing pulmonary edema and acute respiratory distress syndrome.

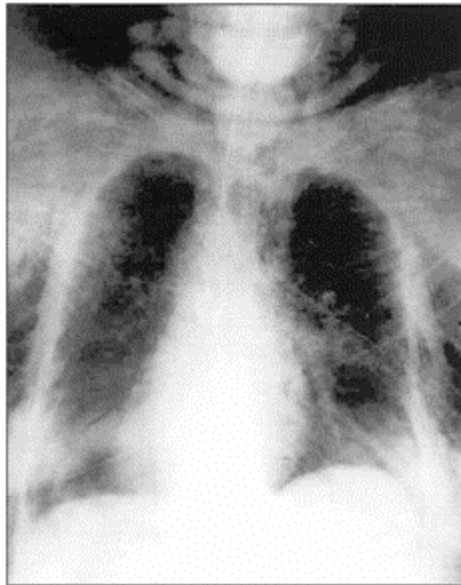
### **Emphysema (subcutaneous/preperitoneal)**

Subcutaneous CO<sub>2</sub> emphysema may be appreciated by the surgical team or anesthetist as crepitance of the skin on the abdomen, thorax, neck, or face. Alternatively, elevations of the ETCO<sub>2</sub> may precipitate evaluation of the hypercarbia (see Table 7.4). While it can occur during removal of the insufflating trocar, it most commonly manifests during Veress needle/trocar insertion.<sup>1,2,51</sup> The Veress needle/ trocar may be improperly placed or CO<sub>2</sub> may inadvertently leak around the trocar.<sup>1,51</sup> The surgical team should be well versed in recognition and malfunctions during insufflation.<sup>51</sup> Preperitoneal needle placement can result in penile and scrotum subcutaneous emphysema. Subcutaneous emphysema during laparoscopy may also result from pulmonary barotrauma associated

with high tidal volumes or increased airway pressures. Clinically, hypercarbia from the subcutaneous absorption of CO<sub>2</sub> may become problematic, necessitating increased minute ventilation, although more frequently it looks worse than it is. No significant hemodynamic sequelae should result, although if accompanied by hypotension, increased airway pressure, or hypoxemia, pneumothorax should be ruled out. The emphysema rapidly resolves and no therapy is typically needed, although subcutaneous IV catheters can be placed or simple skin incisions, 'blow holes', may be created to allow the CO<sub>2</sub> to escape into the atmosphere. Figure 7.4 shows a chest radiograph of a patient with massive subcutaneous gas.

### **Pneumothorax/pneumomediastinum/ pneumopericardium**

Subcutaneous CO<sub>2</sub> emphysema may occur as an isolated phenomenon or more ominously may be the harbinger of pneumothorax (PTX), pneumomediastinum (PMD), or pneumopericardium (PPM). For example, the patient in

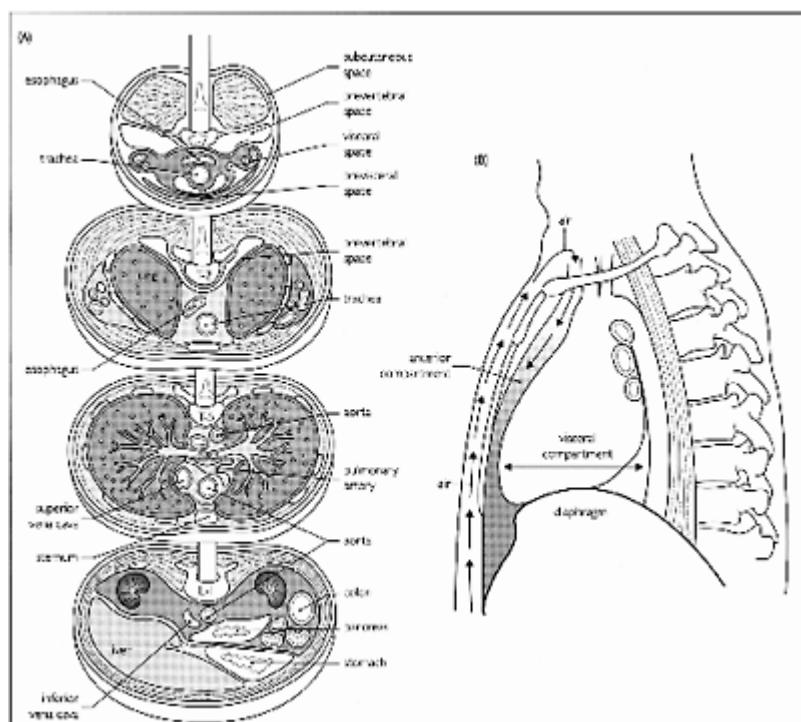


**Figure 7.4** Massive subcutaneous emphysema. This patient developed massive subcutaneous emphysema, which was followed by hypotension and hypoxemia. Bilateral chest tubes were placed with gas release and immediate improvement in hemodynamics and oxygenation.

Figure 7.4 presented initially with massive subcutaneous emphysema but developed hypotension and hypoxemia suggestive of PTX, resulting in bilateral chest tube thoracostomy and subsequent hemodynamic improvement. Similarly, PTX, PMD, or PPM may occur without evidence of each other or subcutaneous emphysema. Isolated PMD and PPM do not typically have significant clinical effects and are found incidentally on postoperative chest X-ray or when patients complain of substernal chest pains.<sup>53</sup> Clinical signs include elevated ETCO<sub>2</sub>, hypotension, hypoxemia, or elevated peak airway pressures (PAWPs), which should prompt the evaluation for potentially catastrophic complications such as a tension PTX. Decreased unilateral or bilateral breath sounds, neck vein distention, and tracheal deviation may not be very sensitive intraoperatively, so high clinical suspicion is needed.

Similar to subcutaneous emphysema, PTX, PMD, and PPM may be the result of pulmonary volume trauma or barotrauma from elevated pulmonary airway pressures. Patients typically have underlying pulmonary disease such as bullous emphysema, bleb disease, pulmonary cyst, or other underlying predisposing condition.

Insufflation of CO<sub>2</sub> can also cause PTX, PMD, and PPM via several mechanisms. Pneumothorax (capnothorax) results from either congenital defects in the diaphragm, diaphragm injury, dissection through fascial retroperitoneal planes, or inadvertent trocar placement into the pleural space.<sup>6,54</sup> Figure 7.5 demonstrates the continuity of the retroperitoneal spaces with the mediastinum, thorax, neck, and chest wall, which is one of the anatomic reasons that explains how CO<sub>2</sub> can dissect through tissue planes to cause PTX, PMD, and PPM. If discovered during positive pressure ventilation or with associated hemodynamic and respiratory compromise, 100% oxygen, discontinuing N<sub>2</sub>O, IV fluid therapy, vasopressor support, hand ventilation, and immediate desufflation should relieve the capnothorax. Many authors note that a capnothorax will resolve within 30 min and no treatment is necessary; however, we believe that if immediate improvement is not seen, needle decompression or chest tube thoracostomy is indicated because pulmonary volume or barotrauma cannot be easily differentiated. Cessation of insufflation



**Figure 7.5** Anatomic fascial planes of the peritoneum, retroperitoneum, mediastinum, and thorax. Fascial planes separating these compartments allow gas to spread through them, depending on the quantity and rate of gas they are subject to as well as the individual integrity of the various layers. The visceral space extends from the retroperitoneum through the diaphragm, mediastinum, and neck. Air originating in any of these structures can dissect into any of the others. (Reproduced with permission from Maunder RJ, Pierson DJ, Hudson LD. Subcutaneous and mediastinal emphysema: pathophysiology,



diagnosis and management. Arch  
Intern Med 1984; 144:1447–53.)

and evaluation prior to continuance is mandatory and conversion to an open procedure may be required. Postoperative discovery is not unusual and because the solubility of CO<sub>2</sub> typically results in rapid resolution mild-moderately symptomatic patients with PTX less than 20% can be managed with observation.<sup>54</sup>

### Hypotension

Hypotension is defined as a fall in arterial blood pressure of more than 20% below baseline or an absolute value of systolic pressure below 90 mmHg or a mean arterial pressure (MAP) below 60 mmHg.<sup>55</sup> Hemodynamic perturbations are common during laparoscopy; however, the incidence of serious cardiovascular complications is low.<sup>1</sup> Hypotension is most frequently caused by a decrease in venous return during development of pneumoperitoneum.<sup>56</sup> However, a thorough differential diagnosis of hypotension in the anesthetized patient undergoing laparoscopic surgery should be considered (Table 7.5) with

**Table 7.5** *Differential diagnosis of hypotension in the patient undergoing laparoscopic surgery*

**Rate/rhythm**

Bradydysrhythmias—CO<sub>2</sub> insufflation, traction on pelvic structures  
Tachydysrhythmias—sinus tachycardia and ventricular dysrhythmias

↓ **Preload**

Hypovolemia  
Caval compression  
Vasodilatation Excessive pneumoperitoneum  
Abrupt change in patient position  
Tension pneumothorax  
Pericardial tamponade

↓ **Contractility**

Hypoxemia  
Myocardial ischemia  
Drug-induced myocardial depression  
RV failure from embolic event  
Acute valve dysfunction  
Severe acidosis  
Abrupt increase in SVR

↓ **Afterload (SVR)**

Drugs  
Distributive mechanisms—sepsis, anaphylaxis, neurogenic, addisonian crisis, transfusion reaction  
Histamine release

↓ decreased; RV, right ventricle; SVR, systemic vascular resistance.

treatment directed by the cause. Most frequently it involves release of the pneumoperitoneum. Vasopressor agents are commonly used to maintain perfusion to the heart and brain, although detrimental in the setting of hypovolemic or hemorrhagic shock. Therefore, vasopressors should be used only to temporize while volume resuscitation is in progress. Atropine is indicated for bradycardia, which is thought to be the cause of the hypotension.

### Hypertension

Hypertension is typically defined as a systolic blood pressure  $>160$  mmHg or diastolic blood pressure  $>90$  mmHg, or both, regardless of age.<sup>57</sup> Severe intraoperative hypertension is rare during laparoscopy.<sup>14</sup> Pneumoperitoneum is the most likely cause and not hypercarbia.<sup>58</sup> Positioning in the head-down position is associated with increased systolic, diastolic, and mean arterial pressure.<sup>59</sup> Several other causes of hypertension such as hypoxemia, and inadequate depth of anesthesia, must always be in the differential diagnosis (Table 7.6). Pre-existing hypertension predisposes to an increased incidence of intraoperative hypertension. Treatment of intraoperative hypertension usually involves deepening the anesthetic but may require the use of sympatholytics. Severe unremitting hypertension may necessitate release of the pneumoperitoneum. Any evidence of ischemia during periods of hemodynamic perturbations should prompt a work-up for significant cardiovascular disease.

**Table 7.6** *Differential diagnosis of intraoperative hypertension in the patient undergoing laparoscopic surgery*

|   |
|---|
| Hypoxemia                                   |
| Hypercarbia                                 |
| Pneumoperitoneum                            |
| Light anesthesia                            |
| Pre-existing hypertension                   |
| Primary                                     |
| Renovascular                                |
| Volume overload                             |
| Drugs                                       |
| Elevated intracranial pressure              |
| Autonomic hyperreflexia                     |
| Malignant hyperthermia                      |
| Endocrine                                   |
| Pheochromocytoma, carcinoid, glomus tumors, |
| thyrotoxicosis                              |

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### Elevated peak airway pressures

Functional residual capacity and lung compliance decrease with pneumoperitoneum.<sup>5</sup> Several studies have documented increased PAWPs during pneumoperitoneum.<sup>2,14,16</sup> The PAWPs increase approximately 50% above baseline values.<sup>5</sup> Interestingly, patients with

documented cardiorespiratory disease did not appear to have significant elevation in PAWPs beyond patients with normal cardiopulmonary status.<sup>8</sup> Position changes such as head-up or head-down do not appreciably alter PAWPs.<sup>16</sup> Other airway misadventures must be in the differential diagnosis of increased PAWPs (Table 7.7). Patients with significant pulmonary disease may manifest marked elevations of PaCO<sub>2</sub> as a result of the ventilator limiting airway pressures, and in some circumstances may make maintaining a pneumoperitoneum difficult. Despite this, patients with significant pulmonary disease should not be summarily dismissed as potential candidates for laparoscopic surgery and they may benefit postoperatively. Fortunately, once the pneumoperitoneum is released, the inspiratory airway pressures return to baseline.

### Hypoxemia

With the institution of the pneumoperitoneum, there is a drop in PaO<sub>2</sub>. This decrease in the PaO<sub>2</sub> rarely results in hypoxemia in ASA I/II (American Society of

**Table 7.7** *Differential diagnosis of intraoperative increased peak airway pressure in the patient undergoing laparoscopic surgery*

***Anesthesia circuit factors***

Kink  
Secretions  
One-way valve malfunction

***Endotracheal tube factors***

Endobronchial intubation  
Secretions  
Kink or patient biting on endotracheal tube

***Patient factors***

Pneumoperitoneum  
Bronchospasm  
Mucous plug  
Pneumothorax/hemothorax  
Pulmonary edema  
ARDS/pneumonia/aspiration  
Poor baseline pulmonary compliance  
    Restrictive lung disease  
    Obesity  
    Kyphoscoliosis  
ARDS, acute respiratory distress syndrome.

Anesthesiology physical classification) patients.<sup>5</sup> There are a few reports that actually demonstrated an increased PaO<sub>2</sub> when local anesthesia was used.<sup>60,61</sup> When hypoxemia does occur, many potential etiologies should be considered (Table 7.8). Baseline decreases in PaO<sub>2</sub> may result in more significant decreases on insufflation. Patients who require home O<sub>2</sub> are at high risk for hypoxemia and may require periodic release of the pneumoperitoneum. Smokers may also be more prone to hypoxemia.<sup>62</sup> PEEP may be useful in increasing MAP, which may improve oxygenation. The immediate treatment of

hypoxemia involves increasing the delivered  $O_2$  to the patient. Some authors advocate a fractional inspired concentration of oxygen ( $FiO_2$ ) of  $>50\%$  to provide an added margin of safety during insufflation.

### Oliguria

Oliguria is defined as urine production at a rate below 0.5 ml/kg/h. Decreased urine output is a common complication of pneumoperitoneum and pneumoretroperitoneum.<sup>63</sup> The mechanism for the decreased urine output cannot simply be explained by decreased venous return

**Table 7.8** *Differential diagnosis of hypoxemia in the patient undergoing laparoscopic surgery*

#### **Hypoventilation**

Esophageal intubation  
Mainstem intubation  
Failure to ventilate  
Airway obstruction  
Pneumoperitoneum

#### **V/Q mismatch**

Mainstem intubation  
Atelectasis  
Pulmonary edema  
Bronchospasm  
Aspiration  
ARDS  
Pneumothorax  
Embolic phenomena

#### **Shunt**

Intrapulmonary  
Intracardiac

#### **Diminished $SVO_2$**

Shock  
Decreased FRC when compared to CC

ARDS, acute respiratory distress syndrome; CC, closing capacity; FRC, functional residual capacity,  $SVO_2$ , mixed venous oxygen saturation; V/Q, ventilation/perfusion.

with subsequent decreased cardiac output. If this were the only factor, expansion of the blood volume should improve urine output. Animal studies have demonstrated that extrarenal pressures as low as 10 mmHg impair renal blood flow and urine production.<sup>39</sup>

Neurohormonal factors probably play a role in the decreased urine output observed clinically. With pneumoperitoneum, plasma renin activity is increased and ADH levels rise.<sup>5</sup> One study found warm  $CO_2$  to be associated with greater urine output.<sup>64</sup>

Anesthetic drugs also decrease renal blood flow, glomerular filtration rate (GFR), and urine output.<sup>65</sup> The decrease in urine output due to anesthetic-related effects can be attenuated by perioperative hydration.<sup>66</sup>

Once the pneumoperitoneum or pneumoretroperitoneum is deflated, an increase in urine output should follow. If prompt improvement of urine output does not occur, a thorough search for other etiologies should be conducted (Table 7.9).

### *Postoperative*

#### **Nausea/emesis**

Postoperative nausea and vomiting (PONV) is one of the most frequent complaints following laparoscopic procedures. Risks for PONV include laparoscopic surgery, female gender, history of PONV or motion sickness, post-operative opioid use, and nonsmoker.<sup>67</sup> An increased number of risk factors correlate with increased incidence of PONV.<sup>68</sup> While PONV is considered a minor complaint, it can be quite distressing to the patient and leads to an

**Table 7.9** *Differential diagnosis of oliguria in the patient undergoing laparoscopic surgery*

#### ***Prerenal***

Hypovolemia  
Decreased cardiac output  
Hypotension

#### ***Intrinsic***

ATN  
Increased ADH  
Glomerulonephritis

#### ***Postrenal***

Obstruction  
Bladder catheter  
Ureteral  
ADH, antidiuretic hormone.

increased length of stay in ambulatory surgical center and to decreased patient satisfaction.<sup>66</sup> Gan has provided useful guidelines for prophylactic antiemetic therapy based on multimodal therapy<sup>67</sup> (Figure 7.6). Other factors that may decrease PONV are stomach drainage<sup>69</sup> and possibly the avoidance of nitrous oxide.<sup>3</sup> Nonopioid analgesics may be beneficial in not only reducing the pain after laparoscopic surgery but may also decrease PONV by minimizing postoperative opioids.

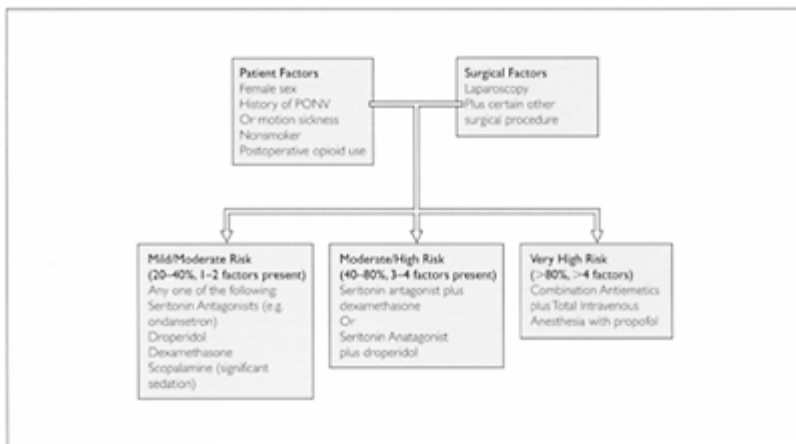
#### **Postoperative pain**

Postoperative pain from laparoscopy is significantly less than laparotomy, although patients can have significant discomfort following laparoscopic procedures. Shoulder and neck pain is reported by a high percentage of patients following laparoscopic procedures.<sup>69</sup> Pain out of proportion to the procedure should prompt an investigation for possible surgical causes (e.g. hemorrhage, bladder perforation, bowel injury, nerve injury).

A variety of techniques are used to minimize discomfort after laparoscopic procedures, including opioids, non-steroidal anti-inflammatory drugs (NSAIDs), local anesthetics, regional anesthesia, and combination therapy. Opioids are effective in alleviating postsurgical discomfort. However, these drugs, in larger doses, have side-effects (PONV, sedation, respiratory depression) that make their use less desirable. The most promising technique for reduction of postoperative pain appears to be multimodal therapy, whereby opioids, NSAIDs, and local anesthetics are used.<sup>3</sup> Other analgesics that can be considered include tramadol and acetaminophen.

### Pulmonary impairment

Postoperative pulmonary complications (PPCs) are an important area of morbidity and mortality in clinical medicine. PPCs comprise a group of events such as pneumonia, respiratory failure, bronchospasm, atelectasis, and hypoxemia.<sup>70</sup> Risk factors for PPCs include surgery lasting over 3 hours, general anesthesia, upper abdominal surgery or thoracic surgery, and intraoperative use of pancuronium.<sup>71</sup> Potential patient-related risk factors include smoking, ASA class greater than II, age greater than 70 years, obesity, obstructive sleep apnea, and chronic obstructive pulmonary disease (COPD).<sup>71</sup> The risk of PPCs is lower in patients who underwent laparoscopic cholecystectomy than those undergoing open cholecystectomy.<sup>71</sup> There are a multitude of studies showing improved postoperative pulmonary function when comparing laparoscopy to laparotomy.<sup>72</sup> Strategies to improve post-operative pulmonary function have been outlined elsewhere.<sup>70,71</sup>



**Figure 7.6** Risk factors for PONV and guidelines for prophylactic antiemetic therapy. Adapted from Gan TJ, Postoperative nausea and vomiting—can it be eliminated? JAMA 2002; 287(10): 1233–6.

## Conclusion

Minimally invasive urologic surgery is increasingly common. The postoperative benefits are less pain, shorter hospital stays, and better postoperative pulmonary function. As more procedures are performed laparoscopically, the anesthesiologist and urologist need to have an understanding of the unique physiologic events that occur as a result of laparoscopy. For the healthy patient undergoing laparoscopy, the cardiorespiratory events are usually little more than minor intraoperative issues. However, for the patient with cardiac or pulmonary compromise the physiologic perturbation can be more severe and requires more preoperative planning.

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## 8

# The physiology of laparoscopic genitourinary surgery

J Stuart Wolf Jr

Laparoscopy may be minimally invasive, but in some ways it is more physiologically stressful on the patient than open surgery. During laparoscopy with gas insufflation, the patient is exposed to physiologic derangements that may be unfamiliar to the operating surgeon. Fortunately, there is now available considerable clinical and experimental research directed towards the physiology and pathophysiology of gas insufflation, and the knowledgeable practitioner can successfully manage most of the physiologic effects of laparoscopy. Prior to the development of operative laparoscopy, diagnostic laparoscopy carried a low 0.6 -2.4% complication rate, and only a third of these could be attributed to physiologic problems.<sup>1</sup> In one large survey of operative laparoscopy (laparoscopic cholecystectomy), one-half of the mortality was due to non-technical ('physiologic') causes.<sup>2</sup> The main purpose of studying this topic is to avoid these physiologic complications.

Most of the work on this topic has concerned intraperitoneal insufflation of gas to produce pneumoperitoneum. Many of the phenomena that have been described likely pertain to gas insufflation into the preperitoneal and retroperitoneal spaces as well; where important differences exist, this will be pointed out, but otherwise the term 'pneumoperitoneum' is used to refer to any gas insufflation for pelvic, abdominal, or retroperitoneal laparoscopy

### **Hemodynamic considerations**

Laparoscopy affects hemodynamics in both stimulatory and inhibitory manners. The mechanical effect of the pneumoperitoneum and the absorption of the carbon dioxide (CO<sub>2</sub>) are the primary determinants of hemodynamic changes associated with laparoscopy. Volume shifts due to positioning of the patient for laparoscopy play a role in some situations. These divisions are useful clinically because each component can be varied independently, allowing the surgeon to alter the patient's hemodynamic response during laparoscopy.

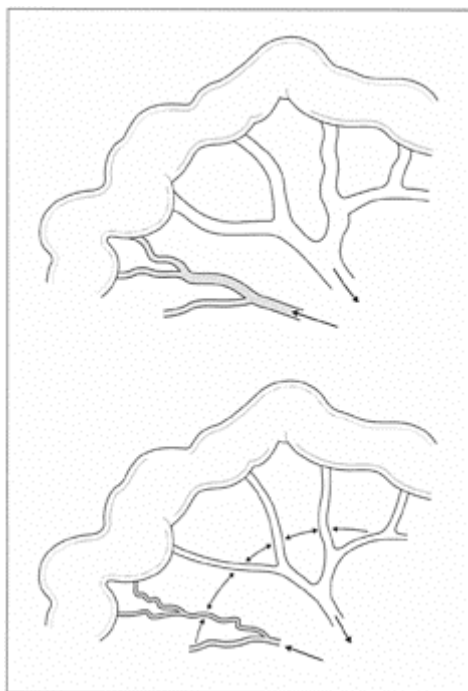
## Physiology

### *Effects of increased intra-abdominal pressure*

Insufflation of gas elevates the intra-abdominal pressure, which subsequently increases the systemic vascular resistance. This is a direct compressive phenomenon, primarily affecting the splanchnic circulation (Figure 8.1),<sup>3</sup> in both capillaries and capacitance vessels, and in both the venous and arterial systems.<sup>4-9</sup> Blood flow to all abdominal and retroperitoneal viscera except the adrenal gland is diminished at 20 mmHg of intra-abdominal pressure in animal models.<sup>3,10,11</sup>

The volume status of the subject determines the magnitude of the effect of intra-abdominal pressure on systemic vascular resistance. Using an intra-abdominal pressure of 20 mmHg in dogs, Kashtan and associates<sup>7</sup> found that cardiac output fell slightly in the presence of normovolemia, decreased significantly with experimental simulation of hypovolemia, and actually increased with experimental simulation of hypervolemia. Others have confirmed the adverse effects of hypovolemia<sup>12</sup> and the beneficial effect of volume loading<sup>13</sup> in the presence of increased intra-abdominal pressure.

Cardiac output is limited by venous return. At low levels of intra-abdominal pressure (less than 10 mmHg), there is augmentation of venous return (and therefore cardiac output), due to 'autotransfusion' from partially emptied abdominal capacitance vessels.<sup>14,15</sup> As intra-abdominal pressures rise above 20 mmHg, venous return and cardiac output tend to decrease (Figure 8.2).<sup>4,6,16</sup>

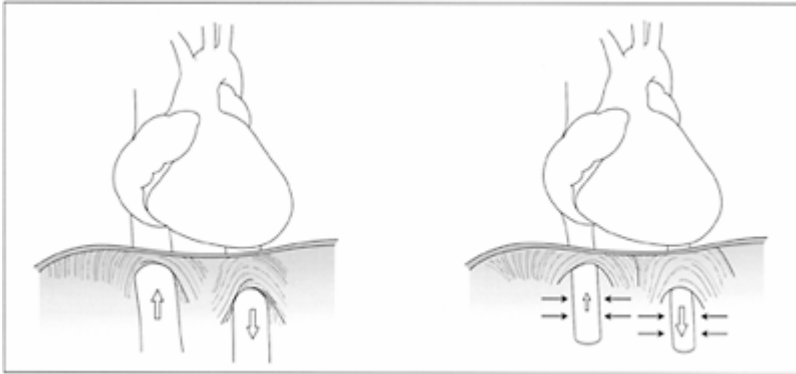


**Figure 8.1** Splanchnic circulation can be markedly restricted. (Reproduced with permission from Wolf and Stoller ML.<sup>1</sup>)

Mean arterial pressure is the product of cardiac output and arterial resistance. At intra-abdominal pressure  $\leq 20$  mmHg, there is elevation of mean arterial pressure.<sup>5,8,9,14–18</sup> With intra-abdominal pressure  $> 40$  mmHg, arterial pressure falls as cardiac output decreases more than arterial resistance rises.<sup>6,19</sup> Venous pressure is determined, similarly, by the volume of blood collected from the capillaries and the venous resistance. As noted earlier, the venous resistance rises with insufflation.<sup>4,14</sup> It is, however, more difficult to measure and interpret venous pressures during laparoscopy compared with traditional open urologic surgery. The central venous pressure measured by a catheter within the right atrium is the sum of intracardiac (transmural) and intrathoracic (pleural) pressures. The former reflects venous return and is the effective cardiac filling pressure. Intrathoracic pressure, which impedes venous return, rises during laparoscopy.<sup>5,7</sup> It is the increase in this component that is the primary reason the measured central venous pressure rises during laparoscopy. Consequently, the measured central venous pressure is not necessarily a good indicator of cardiac filling unless intrathoracic pressure is taken into account.

The complex effects of increased intra-abdominal pressure on hemodynamics are best summarized by considering again the role of volume status. In general, a small increase

in intra-abdominal pressure will increase venous pressure more than it increases resistance, thereby augmenting venous return and cardiac output. As intraabdominal pressure rises above a certain point, the increase in resistance exceeds the increase in pressure and venous return falls. This transition point occurs at a low intra-abdominal pressure in the hypovolemic state because



**Figure 8.2** Reduction of venous return and cardiac output during laparoscopy. (Reproduced with permission from Wolf and Stoller.<sup>1</sup>)

vessels collapse easily. In the hypovolemic state, the transition point occurs at a higher intra-abdominal pressure because the full vessels do not collapse as readily; there is less increase in resistance and the pressure increase remains proportional to the elevation of intra-abdominal pressure. In other words, the balance between resistance and pressure changes that determines venous return—and therefore cardiac output—is dependent upon circulating blood volume. Given the avoidance of hypovolemia, maintaining an intra-abdominal pressure less than 20 mmHg should prevent significant hemodynamic alterations in most patients.

### *Effects of CO<sub>2</sub>*

The insufflated gas is another determinant of the hemodynamic effects of laparoscopy. The absorption of CO<sub>2</sub>, the most commonly used gas, has contradictory effects at different sites. The direct effects of CO<sub>2</sub> are cardioinhibitory, reducing heart rate, cardiac contractility, and vascular resistance.<sup>20</sup> Stimulation of the sympathetic nervous system by CO<sub>2</sub> counteracts these effects, as sympathetic efferents and circulating catecholamines elevate heart rate, cardiac contractility, and vascular resistance. If acidosis develops, parasympathetic stimulation occurs as well.<sup>20</sup> Overall, moderate hypercapnia elevates cardiac output and blood pressure and decreases systemic vascular resistance. The decrease in systemic vascular resistance counteracts the increase created by the mechanical effects of pneumoperitoneum. Insufflation of gases that lack the chemical

activity of carbon dioxide results in a lower cardiac output for a given intra-abdominal pressure.<sup>17,18,21–23</sup>

### *Effects of positioning*

Since laparoscopic retraction can be awkward during laparoscopy, positioning of the patient to use gravity as a retractor is critical. The head-down tilt (Trendelenburg) position during pelvic laparoscopy tends to modestly increase cardiac output.<sup>8,9,24,25</sup> Conversely, the head-up tilt (reverse Trendelenburg) position for upper abdominal laparoscopy is associated with a decrease in cardiac output.<sup>26</sup> The lateral position has minimal effect on hemodynamics unless extreme lateral flexion is applied, which can obstruct the vena cava by impinging on it.<sup>27</sup>

### *Integrated cardiovascular response*

Table 8.1 delineates the hemodynamic effects of an intraabdominal pressure of 15 mmHg and moderate hypercapnia. The response of any individual patient may differ, however. Measured central venous pressure, systemic vascular resistance, heart rate, and mean arterial pressure all increase when CO<sub>2</sub> is insufflated at 15 mmHg pressure, and the effect on cardiac output in this situation in healthy patients ranges from a decrease of 17–19%,<sup>8,16</sup> to no net change,<sup>4,9</sup> to an increase of 7%.<sup>17</sup> Intra-abdominal pressure less than 5–10 mmHg may increase cardiac output in normovolemic patients by 4–15%,<sup>14,15</sup> while intra-abdominal pressure above 40 mmHg risks marked reduction of cardiac output.<sup>4</sup>

### *Retroperitoneal insufflation*

Although not as extensively studied as intraperitoneal insufflation, findings suggest that the impact of retroperitoneal insufflation on hemodynamics is less. In two different experimental studies in pigs, extraperitoneal insufflation tended to alter venous pressures and cardiac output in the same direction but with less magnitude compared to intraperitoneal insufflation.<sup>28,29</sup> Giebler and associates did not find any change in cardiac output up to retroperitoneal insufflation pressures of 20 mmHg,<sup>30</sup> and subsequently confirmed the distinction between

**Table 8.1** *Hemodynamic response to laparoscopy*

|                              | Intra-abdominal pressure<br>of 15 mmHg | Moderate hypercapnia (PaCO <sub>2</sub><br>of 45 mmHg) | Combined |
|------------------------------|--|--|----------|
| Central venous pressure      | Increase                               | Increase   | Increase |
| Systemic vascular resistance | Increase                               | Decrease   | Increase |
| Heart rate                   | Increase                               | Increase   | Increase |
| Mean arterial pressure       | Increase                               | Increase   | Increase |
| Cardiac output               | Decrease                               | Increase   | Variable |

PaCO<sub>2</sub>=arterial partial pressure of carbon dioxide.

intra-peritoneal insufflation (decreased venous return) and retroperitoneal insufflation (slightly augmented venous return) with a clinical study using the same testing methodology in both groups.<sup>31</sup> The smaller volume of gas in the latter group may account for some of the difference.

## Physiologic complications

### *Tension pneumoperitoneum*

When intra-abdominal pressure is excessive ( $>40$  mmHg), the increased vascular resistance becomes overwhelming and tension pneumoperitoneum can occur. Venous return, cardiac output, and blood pressure drop precipitously,<sup>32</sup> which can be fatal.<sup>33</sup> The effect of elevated intra-abdominal pressure is potentiated by hypovolemia,<sup>6,7</sup> so volume status must be optimized before laparoscopy. Parra and associates<sup>34</sup> reported a case of tension pneumoperitoneum during urologic laparoscopy when a malfunctioning insufflator allowed the intra-abdominal pressure to exceed 32 mmHg, resulting in hypotension and bradycardia. Although the procedure was completed following release of the excess pressure and administration of atropine, the patient suffered a cerebrovascular accident that was thought to be due to the intraoperative event. Whenever hemodynamic compromise due to excessive intra-abdominal pressure is suspected, immediate desufflation will quickly improve the situation and the surgeon may be able to complete the procedure at a lower intra-abdominal pressure.<sup>32</sup>

Although brief periods of intra-abdominal pressure above 20 mmHg during laparoscopy are well tolerated by most patients, in general the pressure should be kept below 15–20 mmHg. Even these typically acceptable pressures are no guarantee against problems, as hemodynamic deterioration has been reported at insufflation pressures  $\leq 20$  mmHg.<sup>35</sup> Moreover, patients with cardiac disease, either ischemic heart disease or with congestive heart failure, are at greater risk for intraoperative cardiac dysfunction and should be monitored even more closely.<sup>36,37</sup> Laparoscopy can be performed safely in patients with cardiac ejection fractions less than 15% with careful preparation.<sup>38</sup>

### *Cardiac dysrhythmias*

Cardiac dysrhythmias have been noted during laparoscopy with a frequency of 17–50%.<sup>39,40</sup> Tachycardia and ventricular extrasystoles due to CO<sub>2</sub> are usually benign, but fatal dysrhythmias can occur with very high arterial partial pressure of CO<sub>2</sub> (PaCO<sub>2</sub>).<sup>20</sup> Since hypercapnia may also potentiate parasympathetic actions,<sup>20</sup> vagal stimulation by peritoneal manipulation or distention during CO<sub>2</sub> laparoscopy can occasionally produce bradycardias; asystolic arrest during CO<sub>2</sub> laparoscopy has been reported.<sup>41,42</sup> Avoidance of hypercapnia will prevent tachydysrhythmias. As vagal reactions may be more profound during laparoscopy under local anesthesia, some recommend premedication with atropine in this setting.<sup>43</sup>



*Fluid overload*

The need for intravenous fluid administration is much less during laparoscopy than during open surgery. Not only is the insensible loss of fluid less because there is no body cavity open to air but also urine production is decreased.<sup>44</sup> In one study, urine output during laparoscopy was only 0.03 ml/kg/h, compared to 1.70 ml/kg/h immediately post-operatively, despite an average intravenous intraoperative fluid administration of 13.0 ml/kg/h.<sup>45</sup> An intra-abdominal pressure <10 mmHg caused only mild oliguria, while pressure >10 mmHg produced a 50–100% decrease in urine output in a rodent model.<sup>46</sup> Increased renal vein resistance (with subsequent decreased renal blood flow) and renal parenchymal compression are potential mechanisms.<sup>44,46–50</sup> Pigs exposed to pneumoperitoneum >10 mmHg pressure experienced a 65% fall in urine output, compared to a 29% increase with intra-abdominal pressure  $\leq$  10 mmHg.<sup>51</sup> This combination of decreased insensible losses and decreased urine output predisposes to volume overloading during laparoscopy. In Clayman's nephrectomy series, 2 of the first 10 patients developed transient congestive heart failure, possibly due to administration of excessive intravenous fluid and blood products at a time when the decreased urine output during laparoscopy was not yet appreciated.<sup>52</sup> In an effort to prevent this volume overload, however, patients must not be allowed to become hypovolemic, as this will exacerbate the adverse hemodynamic effect of pneumoperitoneum. The volume status of the patient should be optimized prior to insufflation, and then intraoperative fluid administration should be limited to appropriate replacement for blood loss plus a maintenance rate of 5 ml/kg/h.

*Renal failure*

Corresponding to the decreased urine output during laparoscopy, there is a reduction in creatinine clearance. During laparoscopic cholecystectomy the creatinine clearance fell in 29 of 48 patients in one study, with the decrease being >50% in 8 patients.<sup>53</sup> In a porcine study,<sup>51</sup> the creatinine clearance decreased 18% with intraabdominal pressures  $\leq$ 10 mmHg and 53% with pressures >10 mmHg. Encouragingly, all renal indices returned almost to baseline within 2 hours of the release of pneumoperitoneum. Moreover, the temporary renal insult does not potentiate the toxicity of nephrotoxic agents such as aminoglycosides<sup>54</sup> and even experiments in a chronic renal insufficiency model failed to reveal anything but a transient effect of pneumoperitoneum.<sup>55</sup> If postoperative renal failure occurs in a laparoscopy patient, then other etiologies should be evaluated before ascribing the event to the pneumoperitoneum. Nonetheless, there has been a single case report of acute renal failure lasting for 2 weeks following laparoscopy in a 67-year-old man with chronic renal insufficiency, renal tubular acidosis, and hypertension.<sup>56</sup>

*Hypertension*

Hypertension may accompany hypervolemia during laparoscopy. In addition, hypertension during laparoscopy may be due to hypoxemia, hypercapnia, inadequate anesthesia, or moderately increased intra-abdominal pressure. If hypertension is noted

during laparoscopy, the cuff reading should be verified, the intra-abdominal pressure checked, and the adequacy of anesthesia ascertained. If there is doubt as to the accuracy of pulse oximetry and capnography in estimating the arterial partial pressure of oxygen ( $\text{PaO}_2$ ) and  $\text{PaCO}_2$ , arterial blood gases should be obtained to evaluate for hypoxemia and hypercapnia.

#### *Elevated intracranial pressure and cerebral ischemia*

In a small animal series, the intracranial pressure rose 5 mmHg in pigs exposed to intra-abdominal pressure of 15 mmHg with  $\text{CO}_2$  pneumoperitoneum.<sup>57</sup> In 2 myelomeningocele patients with Arnold-Chiari malformations managed with ventriculoperitoneal shunts, the intracerebral pressure increased more than 15 mmHg above baseline during  $\text{CO}_2$  pneumoperitoneum at  $\leq 10$  mmHg intra-abdominal pressure.<sup>58</sup> In another study of 18 patients with ventriculoperitoneal shunts undergoing 19 laparoscopic procedures, there was no trend toward the combined bradycardia and hypertension that would be expected if this intracerebral pressure increase were clinically significant.<sup>59</sup> Cerebral vascular engorgement secondary to restricted venous outflow is the probable mechanism for the increase in intracranial pressure associated with laparoscopy, although in patients with ventriculoperitoneal shunts distal obstruction of the catheter may play a role as well. Patients with head trauma or cerebral mass lesions may suffer from an increase in intra-abdominal pressure during laparoscopy. As the cerebral circulation responds to the increased intracranial volume and pressure with a decrease in blood flow, patients with significant cerebral vascular disease may suffer ischemia.<sup>60</sup>

#### *Venous thrombosis*

The increased abdominal pressure during laparoscopy restricts lower extremity venous return. Mechanical pressure forces blood out of the splanchnic circulation into the lower extremities.<sup>61</sup> Femoral vein pressures generally parallel intra-abdominal pressures. Lower extremity venous stasis during transperitoneal laparoscopy can be demonstrated with Doppler flow studies.<sup>62,63</sup> One group evaluated femoral vein flow during intraperitoneal and preperitoneal gas insufflation in the same patients, and found flow to decrease with the former but not the latter.<sup>64</sup> Deep vein thromboses and pulmonary emboli have been reported following laparoscopy.<sup>65-67</sup> It is not known if laparoscopy poses a greater or lesser risk for venous thrombosis than open surgery, although in one study of 61 low-risk laparoscopic patients there were no cases of deep venous thrombosis detected with lower limb venous duplex scans.<sup>63</sup> Prophylaxis against deep venous thrombosis with sequential compression devices makes intuitive sense and has been shown to be effective in reversing the pneumoperitoneum-induced reduction of femoral vein flow during laparoscopy,<sup>68</sup> but the optimal method of prophylaxis in laparoscopy has not been determined.

## **Pulmonary, acid—base, and insufflant-related considerations**

Investigations of the pulmonary effects of pneumoperitoneum were first directed toward the use of pneumoperitoneum to treat pulmonary tuberculosis and emphysema.<sup>69</sup> These studies focused on the mechanical aspects of pneumoperitoneum. Subsequently, workers have considered the role of gas absorption from pneumoperitoneum. CO<sub>2</sub>, the most commonly used insufflant, is rapidly absorbed during laparoscopy and consideration of the effects of absorbed CO<sub>2</sub> is important in understanding the physiology of laparoscopy.

### **Physiology**

#### *Mechanical effect of pneumoperitoneum*

Pneumoperitoneum adversely affects pulmonary function. The increased intra-abdominal pressure and volume elevate the diaphragm,<sup>70</sup> reducing both lung capacity and compliance.<sup>15,71</sup> There is worsening of the ventilation/ perfusion mismatch.<sup>70</sup>

#### *Gas absorption*

When the peritoneal cavity is filled with gas by insufflation, the total sum of gas movement is directed outwards into the surrounding tissue because the intra-abdominal pressure is above atmospheric pressure.<sup>72</sup> Individual gases move in a direction determined by their partial pressure gradients. The rate of their movement is determined by:

- tissue permeance of the gas
- absorptive capacity of the surrounding tissue
- temperature
- the area of tissue exposed.

The peritoneal cavity is lined by well-vascularized mesothelium with high absorptive capacity. Gases with high tissue permeance are absorbed readily. CO<sub>2</sub> has the highest tissue permeance of the gases used for insufflation during laparoscopy (Table 8.2).<sup>73</sup> Insufflated CO<sub>2</sub> rapidly diffuses into the bloodstream. The baseline production of CO<sub>2</sub> in adults is 150–200 ml/min.<sup>74</sup> The amount of CO<sub>2</sub> absorbed from the peritoneal cavity during intraperitoneal CO<sub>2</sub> laparoscopy has been estimated to range from 14 to 48 ml/min.<sup>67</sup> Increasing minute ventilation can usually eliminate this excess CO<sub>2</sub>. When the insufflated gas gains access into the extraperitoneal space or subcutaneous tissues, the surface area exposed for gas absorption increases and a greater amount of CO<sub>2</sub> is absorbed.<sup>67,75,76</sup>

*CO<sub>2</sub> metabolism and absorption*

When CO<sub>2</sub> is absorbed or produced by tissue metabolism, it is primarily hydrated to carbonic acid, a reaction catalyzed by carbonic anhydrase. Carbonic acid rapidly ionizes to bicarbonate, which represents 90% of the CO<sub>2</sub> in the bloodstream, and hydrogen ions.<sup>74</sup> The hydrogen ions reduce hemoglobin. In the alveolar capillaries the hemoglobin is re-oxidized and the hydrogen ions are released to produce carbonic acid, subsequently forming CO<sub>2</sub> and water for expiration. If CO<sub>2</sub> elimination cannot keep pace with the sum of metabolic production and absorption of CO<sub>2</sub>, hypercapnia and respiratory acidosis develop. The absolute rise of PaCO<sub>2</sub>, which represents the ‘rapid’ compartment of CO<sub>2</sub> storage, is tempered by storage of CO<sub>2</sub> in the ‘medium’ (primarily skeletal muscle) and ‘slow’ (fat) compartments. These storage sites can hold up to 120 liters of CO<sub>2</sub>.<sup>74</sup> Therefore, all of the absorbed CO<sub>2</sub> is not immediately available for elimination. The situation exists where hypercapnia can develop or persist after the conclusion of an extended laparoscopic procedure.<sup>77</sup>

**Physiologic complications**

*Hypercapnia*

Hypercapnia (excess of CO<sub>2</sub> in the blood) occurs when production and absorption of CO<sub>2</sub> exceed its elimination. While moderate hypercapnia is stimulatory to the cardiovascular system overall, if the level of PaCO<sub>2</sub> exceeds 60 mmHg the direct cardiodepressive effects predominate. Cardiovascular collapse, severe acidosis, and fatal

**Table 8.2** Insufflant characteristics

|                | Solubility <sup>a</sup> | Diffusibility <sup>a</sup> | Tissue Permeance <sup>a</sup> |
|----------------|-------------------------|----------------------------|-------------------------------|
| Nitrogen       | 1.0                     | 1.0                        | 1.0                           |
| Helium         | 0.7                     | 2.7                        | 1.3                           |
| Oxygen         | 1.9                     | 0.9                        | 1.8                           |
| Argon          | 2.2                     | 0.9                        | 2.0                           |
| Nitrous oxide  | 33.0                    | 0.9                        | 28.0                          |
| Carbon dioxide | 47.0                    | 0.9                        | 39.0                          |

Reproduced with permission from Stoller and Wolf.<sup>73</sup>

<sup>a</sup>Value relative to nitrogen.

dysrhythmias can occur. The respiratory acidosis associated with hypercapnia is responsible for most effects of hypercapnia, but CO<sub>2</sub> has direct effects as well. Hypercapnia is related directly to the insufflated CO<sub>2</sub>, and not to any change in tissue metabolism or pulmonary function. In 3 studies comparing N<sub>2</sub>O insufflation to CO<sub>2</sub> insufflation in patients under general anesthesia with controlled respiration at a fixed minute ventilation, the average increase in PaCO<sub>2</sub> was 0.5 mmHg in the N<sub>2</sub>O group and 10.7 mmHg in the CO<sub>2</sub> group.<sup>21,78,79</sup> Animal studies have also confirmed that hypercapnia during laparoscopy is due to absorption of CO<sub>2</sub> rather than mechanical effects on

pulmonary function.<sup>80</sup> The clinical practice during laparoscopy of increasing ventilation rates and tidal volumes in order to increase CO<sub>2</sub> elimination is usually but not always effective. Wittgen and associates<sup>81</sup> converted 2 of 30 laparoscopic cholecystectomies to open surgery because of hypercapnia, and conversion to open surgery because of hypercapnia during laparoscopic pelvic lymphadenectomy has been reported.<sup>65,73</sup> Others have described severe cardiovascular depression or cardiac arrest due to hypercapnia during CO<sub>2</sub> pneumoperitoneum.<sup>41,42,82</sup>

Clinical studies have suggested that subcutaneous emphysema,<sup>67,76,83</sup> elevated intra-abdominal pressure,<sup>4</sup> extraperitoneal insufflation,<sup>67,75,76</sup> and increased duration of insufflation<sup>22,70,79,84</sup> all increase the rate of CO<sub>2</sub> absorption. Other studies have not found extraperitoneal insufflation to be a risk factor.<sup>28,29,85</sup>

Reduction of intra-abdominal pressure is the first maneuver that should be performed when hypercapnia is detected. It allows more effective CO<sub>2</sub> elimination by reducing the mechanical interference with ventilation by pneumoperitoneum, and it decreases CO<sub>2</sub> absorption. Intra-abdominal pressure should be limited to 20 mmHg. In addition, adjustment of ventilation to keep the partial pressure of end-tidal CO<sub>2</sub> (P(et)CO<sub>2</sub>) between 30 and 40 mmHg is recommended. Finally, alternative gases may be employed for insufflation.

Introduced in 1924 by Zollikofer of Switzerland, CO<sub>2</sub> is the most popular gas for insufflation. The advantages of CO<sub>2</sub> are its rapid absorption and its inability to support combustion. The rapid absorption of CO<sub>2</sub> is beneficial if hypercapnia can be maintained at a low level (PaCO<sub>2</sub> ≤ 45 mmHg), because its cardiovascular stimulation offsets some of the hemodynamic burden of pneumoperitoneum.<sup>17,18,21–23</sup> At excessive levels, however, hypercapnia can produce dysrhythmias and cardiodepressive acidosis. For this reason, workers have searched for alternative gases for insufflation. Following the first formal reports of the physiologic hazards of CO<sub>2</sub> pneumoperitoneum,<sup>86</sup> Alexander and Brown described the use of N<sub>2</sub>O for insufflation.<sup>78</sup> N<sub>2</sub>O is similar to CO<sub>2</sub> in that it is rapidly absorbed (see Table 8.2), but it has few physiologic effects at the blood concentration achieved with intraperitoneal insufflation and it is less irritating to the peritoneal membrane.<sup>87,88</sup> Unlike CO<sub>2</sub>, it can support combustion in the abdominal cavity (see Intra-abdominal explosion section below). N<sub>2</sub>O is a suitable alternative for intraabdominal insufflation if electrocautery or laser techniques are not being used.

Other alternative gases include helium (He) and argon (Ar).<sup>23,80</sup> Experiments with He have revealed no cardiopulmonary problems.<sup>80,89</sup> Successful clinical series of laparoscopic cholecystectomy have been performed,<sup>22</sup> and in one case report a laparoscopic nephrectomy associated with extreme hypercapnia was continued safely after switching the insufflatory gas to He.<sup>90</sup> Helium and argon have less chemical activity than CO<sub>2</sub> and are absorbed slowly (Table 8.2). Hypercapnia is obviated by the use of He or Ar for insufflation, but the clinical effects of a venous gas embolism may be exacerbated (see Venous gas embolism section below). A practice of switching to He or Ar after initial insufflation with CO<sub>2</sub> might be a safe and effective way of preventing hypercapnia.<sup>84,90</sup>

Capnography is used to monitor the P(et)CO<sub>2</sub> during operation. The P(et)CO<sub>2</sub>, being about 3–5 mmHg lower than the PaCO<sub>2</sub> during general anesthesia, should be maintained between 30 and 40 mmHg. The difference between PaCO<sub>2</sub> and P(et)CO<sub>2</sub>, the P(a-et)CO<sub>2</sub> gradient, is not significantly worsened during short laparoscopic procedures in healthy

patients.<sup>71,77,91</sup> Normal pulmonary function is adequate to eliminate the small amount of absorbed CO<sub>2</sub> and any increase in PaCO<sub>2</sub> is minimal. As PaCO<sub>2</sub> rises in patients with pulmonary disease, however, P(a—et)CO<sub>2</sub> increases in an unpredictable manner.<sup>81,92</sup> To monitor accurately the CO<sub>2</sub> elimination in patients with pulmonary disease, arterial blood gases may be necessary.

### *Acidosis*

Laparoscopy with CO<sub>2</sub> insufflation causes a mild respiratory acidosis due to the absorption of CO<sub>2</sub>.<sup>6,93</sup> Various investigators have reported coexisting minimal metabolic alkalosis<sup>91</sup> and mild metabolic acidosis.<sup>77,79</sup> Experimentally, the trend towards metabolic acidosis is noted at gas insufflation pressures  $\geq 20$  mmHg.<sup>51</sup> Since the metabolic acidosis is not associated with an increased anion gap, the cause is not likely to be lactate acidosis from splanchnic hypoperfusion, and may instead be related to retained acids due to the decreased urine output at high intra-abdominal pressures.<sup>51</sup>

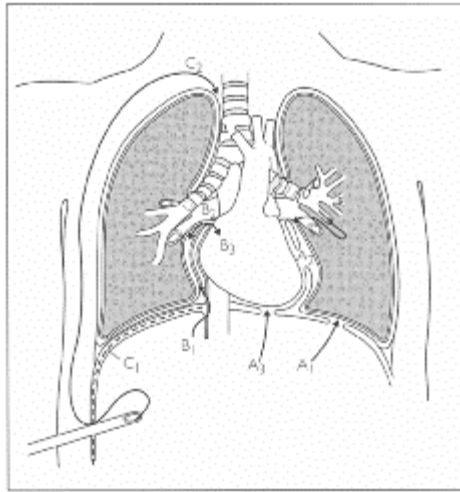
### *Extraperitoneal gas collections*

Gases insufflated into the peritoneal cavity may leak into several extraperitoneal tissue planes or spaces. Subcutaneous emphysema is the most common site of extraperitoneal gas. Its presence is often attributed to technical causes such as incorrect insufflation needle placement, excessive intra-abdominal pressure, a malfunctioning insufflator, or leakage around a laparoscopic port, but in practice it is sometimes inevitable. Since subcutaneous gas is a risk factor for hypercapnia, its presence should prompt an assessment for hypercapnia and its effects. Gas that is insufflated inadvertently into the preperitoneal space or omentum will interfere with visualization during intraperitoneal laparoscopy and might also increase the risk of hypercapnia. Preperitoneal insufflation is a not an uncommon reason for aborting a laparoscopic procedure.<sup>34</sup>

A deliberate extraperitoneal approach is now being advocated for many laparoscopic procedures. Aside from the surgical implications of this approach, there are some physiologic ones. First, extraperitoneal insufflation may be associated with increased gas absorption,<sup>67,75,76</sup> although not all have found this to be the case.<sup>28,29,85</sup> Secondly, extraperitoneal gas can more easily gain access into the subcutaneous space or thoracic cavity. In one study, subcutaneous emphysema was noted in 91% of patients undergoing laparoscopy with extraperitoneal insufflation and in 53% of patients in whom the insufflation was intraperitoneal. Pneumomediastinum or pneumothorax was noted in 36% of patients undergoing extraperitoneal laparoscopy and in 6% of patients after transperitoneal laparoscopy.<sup>67,76</sup>

Pneumomediastinum and pneumothorax can inhibit cardiac filling and limit lung excursion, and can be fatal.<sup>94</sup> Insufflated gas may get into the thorax through many pathways: persistent fetal connections (pleuroperitoneal, pleuropericardial, and pericardioperitoneal), around great vessels in an extrafascial plane, in between fibers of the diaphragm (extraperitoneal or extrapleural), or dissection of subcutaneous gas from the anterior neck directly into the superior mediastinum (Figure 8.3).<sup>1</sup> Pneumothorax may also occur secondary to barotrauma when the peak airway pressure rises with pneumoperitoneum.<sup>71</sup> Pneumomediastinum is more common than pneumothorax, and

when the latter occurs it is almost always accompanied by pneumomediastinum and subcutaneous emphysema.<sup>1,67,76</sup> If CO<sub>2</sub> or N<sub>2</sub>O has been insufflated, the pneumothorax will usually resolve,<sup>95</sup> but thoracostomy should be performed for a large or symptomatic pneumothorax. Pneumopericardium is occasionally noted after laparoscopy.<sup>96</sup> Subcutaneous gas has been present in all reported cases of pneumopericardium, and in 3 of 4 cases there has been radiographic evidence of pneumomediastinum. The mechanism is most likely entry of mediastinal gas into the pericardial space alongside blood vessels, although persistent embryologic pleuropericardial and pericardioperitoneal connections would also allow gas into the pericardium.



**Figure 8.3** Possible routes of gas into mediastinum, pericardial sac, or pleural cavity during laparoscopy include the following: persistent fetal connection at the site of pleuroperitoneal membrane (A1, forme fruste of diaphragmatic hernia), pleuropericardial membrane (A2), and pericardioperitoneal canal (A3); rupture of gas through intact membrane at a weak point such as diaphragmatic hiatus (B1), at pulmonary hilum (B2), and pericardial sac alongside blood vessels (B3); gas outside membrane-bound cavities such as pro- or retroperitoneal gas in

between fibers of the diaphragm or alongside great vessels (C1) or subcutaneous gas from the anterior neck (C2); gas from the rupture of an airspace (barotrauma) enters the mediastinum or pleural cavity by dissecting along the pulmonary vasculature (D). (Reproduced with permission from Wolf and Stoller.<sup>1</sup>)

### *Venous gas embolism*

A venous gas embolism (VGE) is a gas bubble in the venous system that can pass into the heart and pulmonary circulation. The outflow tract of the right side of the heart can be blocked, producing hypoxemia, hypercapnia, and depressed cardiac output. If the right-heart pressure exceeds that on the left side, a probe patent foramen ovale (present in 20–25% of the population) may open and allow embolization of gas into the arterial system.<sup>5,97,98</sup> The incidence of VGE has been estimated to be between 0.002 and 0.08%,<sup>1</sup> although clinically detectable VGE may occur in as many as 0.59% of laparoscopic cases when careful surveillance is used.<sup>99</sup> Many VGE during laparoscopy have been fatal.<sup>97,98,100</sup> VGE rarely occurs more than a few minutes after initial gas insufflation, but delayed cases have been reported.<sup>97</sup> VGE has been produced experimentally in a bleeding vena cava model, with the riskiest situations appearing to be occlusion of the vena cava distal to the venotomy or following significant blood loss.<sup>101</sup> Clinically, VGE should be suspected when there is hypoxemia, evidence of pulmonary edema, increased airway pressure, hypotension, jugular venous distention, facial plethora, or dysrhythmias. The most useful finding is a sudden fall in P(et)CO<sub>2</sub> on capnometry (if the CO<sub>2</sub> embolus is large) and an abrupt but transient increase if it is small.<sup>100,102</sup> The auscultation of a mill-wheel murmur and the appearance of a widened QRS complex with right-heart strain patterns on electrocardiography are less sensitive indicators. When these indicators are noted during initial insufflation, VGE should be suspected. Swift response is required, and includes immediate desufflation, rapid ventilation with 100% oxygen, steep head-down tilt with the right side up, and general resuscitative maneuvers.

The type of the gas comprising the embolus is important. Air (~80% nitrogen) is absorbed very slowly in blood. As Table 8.2 indicates, CO<sub>2</sub> is 47 times more soluble than nitrogen. Graff and associates<sup>103</sup> found the LD<sub>50</sub> (lethal dose in 50% of subjects) of CO<sub>2</sub> to be 5 times that of air when injected intravenously in dogs. Helium, which has been used as an alternative to CO<sub>2</sub> for insufflation in some series,<sup>22,84,90</sup> is even less soluble than nitrogen. In canine experiments, the intravenous injection of He was lethal on 4 of 6 occasions, whereas the same amount of CO<sub>2</sub> was followed by hemodynamic recovery in all cases (Figure 8.4).<sup>104</sup> Additionally, argon VGE during laparoscopic use of an argon beam coagulator has been reported.<sup>105</sup> These findings argue against the use of He or Ar for initial insufflation, but their use after the pneumoperitoneum has been safely created with CO<sub>2</sub> appears safe.<sup>84</sup>

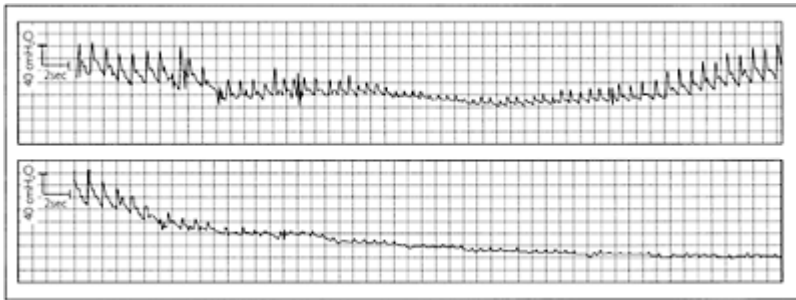


### *Hypoxemia*

$\text{PaO}_2$  may decrease during laparoscopy because of the decreased cardiac output, increased pulmonary shunt, worsened ventilation/perfusion mismatch, decreased alveolar ventilation, and acidosis associated with laparoscopy.<sup>106</sup> Most clinical studies have suggested a slight but clinically insignificant reduction of  $\text{PaO}_2$  during laparoscopy.<sup>6,71,78,81,93</sup> Corall and associates<sup>107</sup> reported that 2 patients with heavy smoking history experienced a drop in  $\text{PaO}_2$  to less than 100 mmHg during  $\text{N}_2\text{O}$  laparoscopy, but others have not found  $\text{PaO}_2$  during laparoscopy to be affected significantly by preoperative pulmonary status.<sup>81</sup> When severe hypoxemia occurs, other complications such as venous gas embolism, pneumothorax, or ventilator malfunction should be considered.

### *Hypothermia*

Hypothermia may occur during laparoscopy because of the loss of heat to the large volumes of gas exchanged through the patient.<sup>108</sup> Ott found that the core temperature dropped  $0.3^\circ\text{C}$  for every 50 liters of  $\text{CO}_2$  used, and recommended warming the gas prior to insufflation to prevent hypothermia.<sup>109</sup> Others, however, found that heating the gas made no difference in the slight drop in core temperature.<sup>110</sup> Moreover, another study found the core temperature to increase rather than decrease during



**Figure 8.4** Arterial tracing after rapid intravenous injection of 7.5 ml/kg  $\text{CO}_2$  (top) and helium (bottom) in a dog. There is recovery within 1 min after the  $\text{CO}_2$  injection but complete cardiovascular collapse after helium injection. (Reproduced with permission from Wolf et al.<sup>104</sup>)

laparoscopy, even with the use of room temperature gas for insufflation.<sup>111</sup>

*Intra-abdominal explosion*

In 1933, Fervers<sup>112</sup> reported an intra-abdominal explosion during laparoscopy with oxygen insufflation, and the use of pure oxygen pneumoperitoneum subsequently has been abandoned. N<sub>2</sub>O will support combustion<sup>113</sup> and is explosive in the presence of hydrogen or methane.<sup>114</sup> Although the proper conditions for explosion during laparoscopy are rare,<sup>115</sup> death has occurred due to cardiac rupture from an explosion during N<sub>2</sub>O pneumoperitoneum.<sup>116</sup> Neuman and associates<sup>117</sup> found that N<sub>2</sub>O content in the peritoneal cavity rose to 36% after 30 min duration of CO<sub>2</sub> pneumoperitoneum when the inhaled gas contained 60% N<sub>2</sub>O. They also reported that 69% hydrogen (the maximum reported content of hydrogen in bowel gas) was combustible in the presence of 29% N<sub>2</sub>O. Therefore, both inhaled and insufflated N<sub>2</sub>O should be avoided when electrocautery or laser might be used. Even without N<sub>2</sub>O insufflation, electro cautery injury to the colon can be associated with explosion.<sup>118</sup>

**Summary**

The hemodynamic effects of laparoscopy are determined by the intra-abdominal pressure, the type of gas insufflated, and the position of the patient. Cardiovascular complications of laparoscopy include tension pneumoperitoneum, cardiac dysrhythmias, fluid overload, renal failure, hypertension, elevated intracranial pressure, cerebral ischemia, and venous thrombosis. The intraoperative pulmonary stresses of laparoscopy can also be considerable. Pulmonary, acid-base, and insufflant-related complications include hypercapnia, acidosis, extraperitoneal gas collections, venous gas embolism, hypoxemia, hypothermia, and intra-abdominal explosion.

Most patients tolerate laparoscopy well if the intraabdominal pressure is limited to 20 mmHg, there is adequate (but not excessive) fluid replacement, and CO<sub>2</sub> levels are monitored appropriately. Nonetheless, it should be remembered that laparoscopy is in many ways associated with more intraoperative physiologic stress than is open surgery. The unique physiologic stresses of laparoscopy require vigilance on the part of the surgeon and anesthesiologist to prevent, monitor for, and treat the potential physiologic complications of laparoscopy.

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## 9

# Physiology of endoscopic surgery

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### Introduction

Disorders of fluid and electrolytes are normally controlled by multiple homeostatic mechanisms. These mechanisms can be easily overwhelmed by acute and chronic disorders of the renal, cardiopulmonary, vascular, and neuroendocrine systems. This chapter describes surgical causes of fluid and electrolyte disorders, specifically those related to urologic endoscopic surgery.

In normal adults, total body water makes up approximately 60% (50% in females) of total body weight. This water is divided into intracellular and extracellular compartments (Figure 9.1). The principal intracellular solute is potassium; the principal extracellular solute is sodium. The plasma component of the extracellular fluid helps to maintain filling pressures in the circulatory system. Alterations in sodium and water balance play vital roles in maintaining these pressures.<sup>1-3</sup>

| Fluid compartment breakdown in a 70 kg man |  |
|--|--|
| • Total body water                         |  |
| – 60% of total weight                      |  |
| – 40 liters                                |  |
| • Intracellular fluid                      |  |
| – 66% of total body water                  |  |
| – 26 liters                                |  |
| • Extracellular fluid                      |  |
| – 33% of total body water                  |  |
| – 14 liters                                |  |
| • Plasma                                   |  |
| – 20% of extracellular fluid               |  |
| – 3 liters                                 |  |
| • Interstitial fluid                       |  |
| –80% of extracellular fluid                |  |
| –11 liters                                 |  |

**Figure 9.1**

Body fluid compartments.



Endoscopy can lead to hypervolemic/dilutional hyponatremia because large amounts of osmotically active irrigants are absorbed. The principal sequela of the physiologic effects of urologic endoscopic surgery are volume-expanded states characterized by an increase in total body water and concomitant hyponatremia.

Clinically, certain factors contribute to volume overload and resulting dilutional hyponatremia. These factors place patients at higher risk of developing signs and symptoms because they are more susceptible to fluid shifts and cannot compensate as well. These factors include:

1. cardiac disease
2. vascular nephropathies causing salt wasting;
3. hydronephrosis, which can create a salt-wasting kidney
4. acute urinary retention, i.e. benign prostatic hyperplasia (BPH)—which can lead to a salt-wasting diuresis
5. general chronic illnesses, which lead to poor nutrition, anemia, and reduced total body water.<sup>4</sup>

Volume overload and dilutional hyponatremia have the most significant effects intracranially. An increase in cerebral intravascular volume with hypotonic fluid causes cellular edema and increased intracranial pressure. Symptoms of cerebral edema include hypertension, bradycardia, nausea, emesis, headache, convulsions, and coma. Other significant effects are also seen in the lungs, where swelling in the interstitial alveolar spaces decreases oxygen exchange and leads to shortness of breath and cyanosis.

### **Irrigants used in endoscopic procedures**

The key properties of an irrigant to consider during endoscopy are optics, risk of intravascular hemolysis, and ability to conduct electricity. During percutaneous nephrolithotomy (PCNL) and ureteroscopy (URS), normal saline is the best choice because it is isotonic. However, it cannot be used during transurethral resection of the prostate (TURP) and transurethral resection of bladder tumor (TURBT) because the ions disperse the current.

Initially, distilled water was used as an irrigant because it lysed the red cells and improved vision. However, hemolytic reactions occurred and were sometimes fatal because of jaundice and kidney failure from hemoglobinemia.<sup>5</sup> A 5% glucose solution prevented intravascular hemolysis but was not optimal because of poor visualization during resection.<sup>6,7</sup> Glycine, sorbitol, and mannitol are electrically nonconducting, osmotically active solutes that are added to irrigation fluids to decrease the risks of massive intravascular hemolysis and are now the mainstay of endoscopic surgery when electrocautery is required.

Glycine was one of the first nonelectrolyte solutes used and has been utilized in several concentrations. Glycine (1.1%) leads to an increased risk of hemolysis and provides minimal protection from TUR syndrome. Glycine (2%) causes significant central nervous system (CNS) symptoms. Glycine (1.5%) is the preferred concentration.<sup>8</sup> It is the most widely used irrigant in the world, although it is associated with more serious side-effects than mannitol and sorbitol.<sup>9</sup> The toxic effects that have been reported

include bradycardia, hypotension, transient blindness, and chest pain.<sup>8,10,11</sup> In animal studies, glycine may induce cardiac stress as a result of ischemic damage to myocardial cells. Others report an increased risk of myocardial infarction, although further studies are necessary.<sup>12-14</sup> Glycine adversely affects hemodynamic variables but the mechanism is unclear. Similar hemodynamic effects have also been reported with sorbitol and mannitol.<sup>9,12,15</sup> Glycine causes CNS abnormalities because of its actions as an inhibitory neurotransmitter.<sup>16</sup> Hyperammonemia can also result with absorption of large amounts of glycine because the nitrogen component of glycine cannot be completely metabolized. Glycine intoxication can overload the Krebs cycle and leads to encephalopathy.<sup>17</sup>

Mannitol (3%) and sorbitol have been extensively studied and are thought to have properties similar to those of glycine in terms of optics, conductivity, and nonhemolyzing effects. They are thought to have no known cardiotoxic effects and theoretically could cause fewer adverse effects.<sup>9,18</sup> In fact, mannitol may be protective because of its diuretic effect. Excessive diuresis, leading to hypotension from both mannitol and sorbitol, and sorbitol-induced lactic acidosis, has not been shown to have clinical significance. One case report suggested sorbitol as the cause of severe hyperglycemia.<sup>19</sup> Although combined solutions of mannitol and sorbitol have been studied, there is no strong evidence proving that glycine, sorbitol, mannitol, or a combination is more efficacious.<sup>9,18,20,21</sup>

Although these solutions are isotonic or slightly hypotonic, absorption of these irrigants is still associated with adverse effects, including TUR syndrome. The hyponatremia caused by these irrigants may not be due to dilution alone. All of these irrigants can also cause an osmotic diuresis that is associated with an obligatory sodium loss in the urine. Thus, there may also be a true sodium depletion in addition to water intoxication. Finally, these irrigants cause cellular swelling despite their relative iso-osmolality because glycine and sorbitol diffuse into cells (not mannitol), are followed by water, and are then metabolized intracellularly.

## **Metabolic consequences of endoscopic urologic procedures**

### *Transurethral resection of the prostate*

TURP syndrome results from intravascular absorption of large volumes of irrigation fluid through venous sinuses in the prostatic bed and via periprostatic tissue if the capsule is penetrated. In one large study, the incidence of TUR syndrome was 2% of patients.<sup>22</sup>

Reports of TUR syndrome began around 1946.<sup>5,23</sup> A variety of clinical manifestations were reported: hypertension (secondary to volume overload), bradycardia, dyspnea, cyanosis, visual changes, nausea, emesis, irritability, confusion, coma, and death (<1% of cases). Obviously, these symptoms can be recognized during the procedure only if a regional anesthetic is used; thus, many physicians are prompted to recommend regional techniques for TURR.

Initial hypotheses of the pathophysiology of TUR syndrome included side-effects of preoperative medication, anesthesia, blood loss (hypovolemic shock), myocardial infarction, cerebrovascular accident, and pulmonary embolism. Today, most agree that the pathophysiology of TUR syndrome is related to dilutional hyponatremia from water

intoxication. This is most commonly seen in patients with pre-existing electrolyte and extracellular fluid deficiencies because they are less able to readily distribute the excess fluid between the three compartments. Hemolytic reactions have also been reported with the use of water as an irrigant and result in acute renal insufficiency secondary to hemoglobinemia and cardiac arrest secondary to hyperkalemia.

Absorption of large amounts of iso-osmolar irrigant during TURP causes a significant and rapid increase in intravascular volume and changes in the concentration of solutes in serum. The clinically evident effects of dilutional hyponatremia usually do not occur until sodium is less than 125 mEq/L (and are more pronounced with a rapid fall). The absorption of fluid occurs during almost every TURP. The uptake of 1 L of irrigant corresponds to a decrease of up to 5–8 mmol of serum sodium in a 70 kg man. This amount of fluid absorption has been shown to occur in up to 10% of all TURPs performed.<sup>8</sup> The initial transitory hypertension is thought to be due to the rapid increase in the intravascular volume and is related to an associated reflex bradycardia (baroreceptors).<sup>24</sup> Shortness of breath and respiratory distress are also due to rapid intravascular expansion because increased central venous pressure leads to left ventricle overload, which in turn leads to pulmonary edema.<sup>24,25</sup> Capillary hydrostatic pressure is increased and oncotic pressure decreased due to protein dilution. Eventually this causes movement of fluid from the high-pressure, low-solute intravascular space out of the capillaries and into the interstitial space, leading to tissue swelling and, ironically, relative hypovolemia. In the closed space of the CNS, this results in cerebral edema and elevated intracranial pressures with the resulting clinical sequelae.

A risk factor that can be assessed preoperatively is prostate gland size. In a large retrospective cooperative study, a prostate size of 45 g or greater was shown to increase the risk of TUR syndrome.<sup>22</sup> Variables that also play a role include type of irrigation, height/pressure of fluid, length of resection (> 60–90 min), completeness of resection/number of open sinuses, and intrabladder pressures.<sup>24,26,27</sup>

The importance of the influence of pressure in the prostatic fossa to absorption has been well studied. In a randomized prospective study, Madsen determined that a critical pressure range existed. By lowering the height of the irrigation bag from 70 to 60 cm, the total absorption could be reduced by almost 50%. From radioisotope studies, Madsen determined that this pressure limit was approximately 30 mmHg, which corresponds to approximately 60 cmH<sub>2</sub>O. Therefore, the critical height of the irrigation should not exceed 60 cm above the operating room table. Above that height, significant absorption of irrigation fluid occurs.<sup>28</sup> In addition, it is important to keep the pressures low as long as possible by partially opening the stopcock for the inflow and to empty the bladder frequently. This can be facilitated by continuous flow resectoscopes and placement of a suprapubic tube.

Some authors argue that even with the uses of intermittent irrigation, suprapubic drainage, or continuous flow resectoscopes, the pressures are still higher than in the pelvic veins. They claim that in theory these techniques should help decrease absorption but in reality there is too much difficulty maintaining an accurate balance between inflow and outflow of fluid.<sup>29,30</sup> Others have contested the existence of a correlation between the height of the irrigating fluid and absorption.<sup>31</sup>

Fluid absorption during resection of bladder tumors is rare. In one study investigators reported on 40 patients who underwent extensive resection for large-volume tumors. They measured fluid absorption using ethanol in the patients' expired breath. The study concluded that none of the patients absorbed the irrigation fluid.<sup>32</sup>

Others have reported on individual patients with TUR syndrome.<sup>33</sup> They concluded that absorption was most likely through the extravascular route. Fluid absorption through the bloodstream is unlikely with TURBT and more likely to be due to perforation of the bladder. This pattern causes a delayed hyponatremia and a different clinical picture than previously described. Abdominal pain usually occurs and is followed by nausea, emesis, hypotension, and general signs of fluid overload, which is usually delayed due to extravascular absorption via the peritoneum rather than the more rapid intravascular absorption.<sup>24</sup> Hahn believes that, paradoxically, hypovolemic hyponatremia can occur because the solutes from the irrigant are in the interstitial compartment. Therefore, water equilibrates by diffusing from the intravascular space to the interstitium. The paradoxical effect is that total body fluid overload has occurred with resultant intravascular hypovolemia. Therefore, treatment by diuresis would be unwise. Understanding the patient's volume status and the physiology of hyponatremia is of paramount importance.<sup>33</sup>

Dilutional hyponatremia has also been reported and is thought to occur via bleeding vessels from the bladder tumor resection.<sup>33</sup> Intrabladder pressure <15 mmHg does not cause significant absorption of irrigating fluid, although significant absorption does occur at pressures <30 mmHg.<sup>24</sup>

### *Ureteroscopy and percutaneous nephrolithotomy*

During PCNL and URS, absorption of fluid can occur if perforation and extravasation occur with absorption through the peritoneum. A second means more unique to PCNL and similar to TURP is the absorption of fluid through open venous sinuses in the kidney caused by dilation while the surgeon is gaining access to the collecting system. A major factor preventing a TUR-like syndrome and more frequent hyponatremia is the use of normal saline for the irrigation fluid. Since electrocautery is rarely used, nonconducting irrigants are not necessary. Therefore, normal saline can be used equally well and more safely than glycine.<sup>34</sup>

During PCNL, the irrigating pressures are kept low by using a large sheath to access the kidney. This alleviates high pressures and absorption through the large venous sinuses. There is little evidence of significant fluid absorption during PCNL.<sup>35</sup> In 148 cases, fluid absorption was evident in all patients and the maximum fluid absorbed was 474 ml. No patients had evidence of fluid overload or electrolyte imbalance. However, patients with compromised cardiopulmonary or renal function should be watched closely because fluid absorption does occur and these patients may not be able to handle the volume shifts as well as others.

The risk of absorption of large amounts of fluid during ureteroscopy is greatly reduced because the instruments used are of a significantly smaller caliber and result in lower flow rates and less irrigation.

## Treatment

Treatment of TUR syndrome is aimed at early awareness of the symptoms (a high index of suspicion is the key to early diagnosis). After termination of the procedure, treatment consists of replacement of lost blood, restoration of normal circulating plasma volume, and correction of electrolyte abnormalities.

To manage patients with TUR syndrome effectively and safely, clinicians must determine the volume status of patients and estimate the sodium deficit. In addition, they must consider the chronicity of the situation, as it has major implications in determining the appropriate speed for correcting the sodium deficit and the degree of distribution of the problem. With the rapid infusion of fluid deficient in sodium into the intravascular fluid compartment, this fluid diffuses into the extracellular fluid over a period of hours. Over the ensuing hours, there is a movement of water from the extracellular fluid compartment to the intracellular fluid compartment, with resultant cellular swelling. When this occurs in the brain, cerebral edema ensues with its attendant sequelae. When this problem occurs more gradually, as in the patient with chronic hyponatremia as a result of diuretic use, the brain accommodates by decreasing intracellular osmolality and minimizing cellular effects. If the osmolar imbalance in TUR syndrome is not corrected quickly, however, further cellular swelling will result and the clinical condition will deteriorate. Conversely, if the hyponatremia of chronic diuretic use is corrected too quickly when the brain cells have already adjusted to the chronic hyponatremic condition, cellular shrinkage will occur with its own attendant risks, i.e. central pontine myelinolysis. As a general rule, the deficit should be corrected over a time period similar to the time period over which it developed.

In most cases of TUR syndrome, there is a volume overload condition and it is appropriate to initiate a diuresis. This is most conveniently done with the administration of furosemide. When the volume status is unclear or cardiac instability has developed, central cardiac monitoring may be appropriate. Furosemide results in both sodium and water diuresis. However, the degree of water diuresis exceeds the sodium diuresis and this begins to address the water intoxication by inducing a relative water loss.

In severe cases in which CNS symptoms have developed, a more precise approach to treatment is appropriate and the relative sodium deficits and water excesses should be calculated. Sodium is the major determinant of plasma osmolality (Figure 9.2) and is normally distributed through all of the extracellular fluid compartment. The kidney normally regulates sodium by increasing or decreasing 'free water.' This term refers to the amount of solute-free water that has to be added to or subtracted from urine to make it iso-osmolar to serum. Thus, the addition of free water to serum, either by a failure to excrete free water by the kidney or by an increase in the absorption of free water, causes a decrease in serum sodium.<sup>1</sup> Excessive absorption of fluid during endoscopic procedures can easily cause an acute decrease in serum sodium (hypo-osmolar hyponatremia), usually  $<120$  mEq/L. The goal is to correct total body water osmolality to approximately 250 mOsm/kg. The desired target serum sodium level for correcting the condition is typically 125 mEq/L, which equals 250 mOsm/kg when sodium's anion (chloride) is factored in. In the TUR syndrome scenario, changes in serum sodium directly reflect the changes in total body water. A low concentration of sodium does not always mean the patient has excess free water. For example, hyponatremia can also be due to:

1. increased plasma osmolality due to poorly controlled diabetes
2. volume depletion due to diarrhea or diuretics; or
3. volume excess due to edema (i.e. congestive heart failure, cirrhosis, or nephrotic syndrome).<sup>1,3</sup>

In the setting of TUR syndrome, however, the hyponatremia is primarily the result of the sudden addition of the fluid to the total body water that is deficient in sodium. This is not really a deficiency of sodium but an excess of

$$\text{Posm} = (2 \times \text{pNa}^+) + \text{glu}/18 + \text{BUN}/3$$

- Urea can be eliminated because it is not osmotically active

## Figure 9.2

Normal plasma osmolality.

Posm=plasma osmolality, BUN blood urea nitrogen,  $\text{pNa}^+$ =plasma sodium, glu=plasma glucose.

water in the absence of sodium. While this problem is primarily one of water intoxication, the clinician has no way of rapidly removing the excess free water (other than dialysis) and must address the problem by adding sodium to the body water in order to restore serum sodium levels to more normal levels while diuresing the patient to eliminate the excess volume that results. Correction of serum sodium requires the calculation of the sodium deficit (Figures 9.3–9.6). In TUR syndrome, the sudden decrease in serum sodium causes ongoing cellular swelling and progressive neurologic compromise until an equilibrium has been established. However, while the water intoxication is spread through all of the body fluid compartments, equilibration has not been reached and it is appropriate to replace the ‘sodium deficit’ only partially to prevent overshooting and causing the reverse problem of sodium overload. In most cases, the clinician would replace half of the calculated deficit over 1–2 hours. In contrast to chronic hyponatremic conditions, it is important to return sodium levels to near normal levels as rapidly as possible. This is accomplished with the infusion of hypertonic saline (usually 3% (514 mEq/L)). Figure 9.5 demonstrates how to calculate the desired volume of hypertonic saline to be infused in a patient experiencing the full manifestation of TUR syndrome. A target sodium of 125 mEq/L is chosen in order to account for the fact that complete equilibration has not occurred and to prevent overshooting the desired serum sodium concentration. In most cases, correction of the serum sodium to this level will eliminate any neurologic conditions. In extreme cases of fluid absorption that

$$\text{Na}^+ \text{ deficit} = (\text{Desired serum Na}^+ - \text{Measured Na}^+) \times \text{TBW}$$

- TBW (total body water) =  $0.6 \times \text{weight (kg)}$ 
  - 60% (0.6) in males
  - 50% (0.5) in females

## Figure 9.3 Calculation of sodium deficit.

$$\text{Excess H}_2\text{O} = \text{TBW} \times [\text{I} - (\text{Actual Na}^+ / \text{Desired Na}^+)]$$

**Figure 9.4** Amount of free water that must be excreted to correct sodium.

TBW=total body water.

$$3\% \text{ saline (L)} = [\text{TBW} \times (\text{Desired Na}^+ - \text{Actual Na}^+)] - 514 \text{ mEq}$$

- 514 mEq=total mEq in 3% saline
- Desired sodium concentration=125 mEq

**Figure 9.5** Liters (L) of 3% saline required to correct hyponatremia.

TBW= total body water.

A 65-year-old healthy male (75 kg) with BPH undergoes TURP and shortly after the procedure has a brief episode of bradycardia, is nauseated, and confused. Serum electrolytes are sent and his  $\text{Na}^+$ =105 mEq/L How much hypertonic saline is required to correct this patient's  $\text{Na}^+$ ?

- The goal of the acute treatment is to ameliorate but not completely correct the hypotonic state
- $\text{TBW} = 60\% \text{ of body wt} = 0.6 \times 75 \text{ kg} = 45 \text{ L}$
- $\text{Na}^+ \text{ deficit} = (\text{desired Na}^+ - \text{actual Na}^+) \times \text{TBW}$   
 $= (125 \text{ mEq/L} - 105 \text{ mEq/L}) \times 45 \text{ L}$   
 $= 900 \text{ mEq}$
- If 1L of 3% saline has 514 mEq then the amount of 3% saline (x) to provide 900 mEq:  
 $\rightarrow 514(x) = 900$   
 $\rightarrow x = 1.7 \text{ L}$
- Therefore 1.7 L of 3% saline should be infused at a rate no greater than 25 mEq/h so as not to correct serum sodium too quickly

**Figure 9.6** Example of how to correct sodium levels in a patient with dilutional hyponatremia. BPH=benign prostatic hyperplasia, TURP=transurethral resection of the prostate.

do not respond to the above treatments, acute hemodialysis should be instituted.

Figure 9.6 demonstrates an example of an acute dilutional hyponatremic state from TURP. After the sodium deficit is calculated, half of the hypertonic saline should be infused. Electrolytes should then be redrawn and the sodium deficit recalculated before continuing treatment. If hyponatremia results from a chronic condition, replacement should be at a slower rate to prevent central pontine myelinolysis. As a general rule, the sodium deficit should be corrected over the same time frame as it developed.<sup>2</sup>

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## 10

# Laparoscopic access, trocar placement, and exiting the abdomen

Sean P Hedican and Stephen Y Nakada

### Introduction

Proper access to the peritoneal cavity or retroperitoneum, including the insertion and positioning of port sites, is as important as the laparoscopic procedure itself for insuring a good surgical outcome. In a recent review, initial access to the peritoneal cavity accounted for anywhere from 6% to 57% of injuries occurring during laparoscopy.<sup>1</sup> In addition, poor trocar planning can result in unnecessary frustration due to crossing of instruments, difficult angles of approach, mirror imaging, and shoulder fatigue. Diligence should also be exercised in exiting the abdomen to prevent inadvertent organ injury and delayed complications (abdominal wall bleeding and/or trocar site hernia formation). This chapter outlines the critical elements involved in safe and effective laparoscopic access, trocar placement, and exiting the abdomen, with emphasis on ways of avoiding potential pitfalls.

### Accessing the abdomen

#### *Closed transperitoneal access*

Closed laparoscopic access to the peritoneal space is most commonly obtained after initial insufflation via a Veress access needle. The needle is usually inserted at the region of the umbilicus for procedures performed in the supine position. At the umbilicus, the puncture is concealed and there are no intervening layers of muscle encountered, so the Veress needle only has to pass through the fused anterior and posterior rectus sheaths before entering the peritoneum. For flank access, we prefer inserting the Veress needle via the trocar skin incision made for the lower quadrant port of the ipsilateral side of the pathology. Caution should be exercised not to insert the needle too laterally, in close proximity to the superior iliac crest, because this can result in retroperitoneal insufflation or puncture of the colon (sigmoid on the left and the cecum on the right).

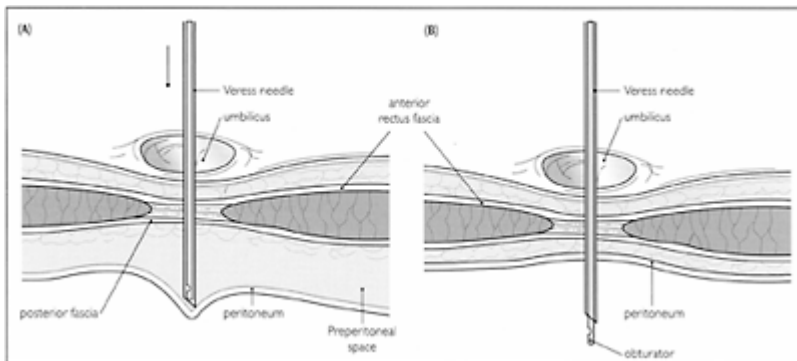
Key steps to insure correct intraperitoneal insertion and avoid injury to underlying viscera or vasculature include insertion of the Veress needle perpendicular to the fascial surface while tenting up the abdominal wall using instruments or manual elevation. Passage through two points of maximum resistance are noted as the needle traverses the fascial layers with less resistance as it passes through muscle and fat. An audible snap of the internal obturator heralds entry into an area of low resistance, which is usually the

peritoneal cavity (Figure 10.1), and further advancement of the needle is halted. Intraperitoneal localization is confirmed by:

1. a lack of resistance with gentle side-to-side movements of the needle tip
2. easy injection and drainage of saline through the hub of the Veress needle
3. lack of succus entericus, blood, or air on gentle aspiration with a 10 ml syringe attached to the Veress needle
4. low insufflation pressures ( $<10$  mmHg) at a low flow rate.

It is important to take into account body habitus when assessing the appropriateness of observed insufflation pressures. Obese patients with a large amount of chest and abdominal wall fat may have a resultant increase in their intraperitoneal pressure. Initial recordings in these patients may be just under 10 mmHg at low insufflation rates and remain stable until the peritoneal cavity nears complete distention.

If all of the localization findings occur as noted above, yet the recorded intraperitoneal pressures appear inappropriately high, or occlusion alarms intermittently sound, then the needle may be entrapped in omentum or bowel mesentery. Gentle incremental withdrawal or angulation



**Figure 10.1** (A) Veress needle being inserted with initial retraction of the internal obturator on contact with the skin or fascia. (B) On entry into the peritoneal cavity, the protective obturator snaps forward with an audible engagement to protect the underlying viscera and vasculature.

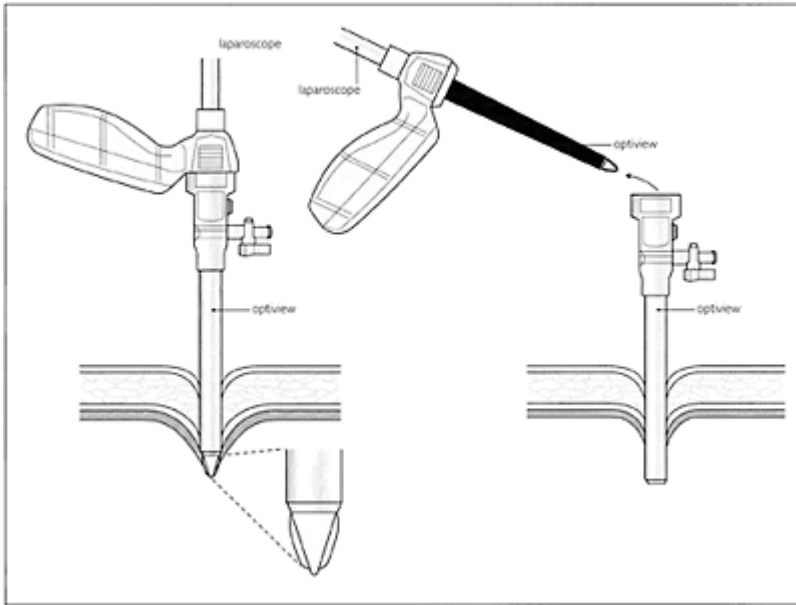
of the needle is safe to perform with repeat inspection of the pressure after each adjustment. If pressures do not improve, the needle should be removed and reinserted.

After establishment of the pneumoperitoneum at 15–20 mmHg pressure, either a blind or visual trocar technique can be utilized for introduction of the initial port. A blind trocar technique involves insertion of the initial port, utilizing either a fascial cutting or splitting

trocar, with entry into the peritoneum determined by both a loss of resistance and audible engagement of the inner protective obturator. Final confirmation is obtained by venting the port or performing a direct camera inspection of the peritoneal contents. The risk of inadvertent injury to underlying viscera or catastrophic vascular injury when utilizing this technique is obviously higher than what is observed using direct vision trocar methods.<sup>1</sup>

Direct vision port introduction utilizes a pistol-shaped introducing obturator with either a fascial splitting clear plastic point (e.g. Optiview, Ethicon Endo-Surgery, Cincinnati, Ohio) (Figure 10.2) or a fascial cutting blade which is activated each time the trigger is pulled (Visiport, U.S. Surgical (USSC) Norwalk, Connecticut) (Figure 10.3). The Optiview comes in both a 10/12 mm pistol as well as a 5 mm size that is shaped like a standard obturator through which a 5 mm laparoscope may be introduced. Once the laparoscope is inserted and focused on the line traversing the plastic tip of the Optiview, it is slowly advanced using a back-and-forth twisting motion through the layers of the abdominal wall. Each layer can usually be identified as it is traversed. Entry into the peritoneum is recognized initially as a widening dark hole through which the trocar is advanced. Once inside the peritoneum, the visual obturator is removed from the port and taken off of the laparoscope (Figure 10.2). The Optiview, like other non-cutting trocars, splits the fascia along the course of its fibers and, theoretically, has less chance of postoperative hernia formation even without fascial closure.<sup>2</sup> In contrast, the Visiport device has a blade that cuts the fascia and only comes in a 12 mm size. Since it is desirable to cut the fascia along the course of its fibers, the camera of the laparoscope is focused on the blade of the Visiport, which is then oriented in the direction of the fibers by turning the end of the pistol grip handle. As the trigger is depressed and each layer of the abdominal wall is cut, the device is slowly advanced with a twisting motion until it enters the peritoneal cavity. Larger abdominal wall vessels can usually be visualized with this device and avoided by changing the orientation of the blade so it runs parallel and to the side of the vessel.

The use of a visual obturator without prior insufflation has also been described. The theoretic risk for injury to underlying structures is higher due to the lack of separation between the parietal peritoneum and the underlying viscera. In this closed transperitoneal access technique, the visual obturator is utilized in exactly the same fashion as it is with an insufflated abdomen; however, entry into the peritoneum is confirmed by loss of resistance and the visual appearance of bowel or omentum.



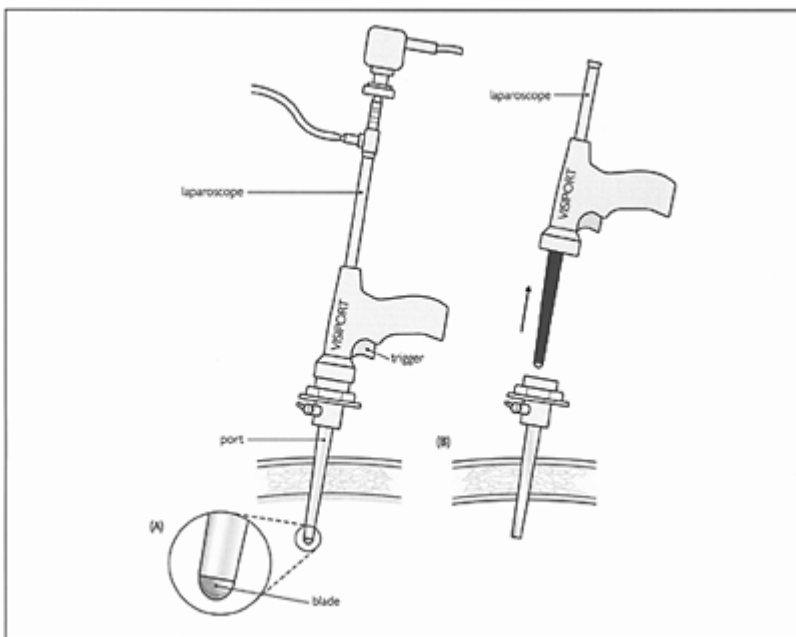
**Figure 10.2** (A) 10/12 mm Optiview cannula (Ethicon Endo-Surgery, Cincinnati, Ohio) with its fascial splitting point being introduced. (B) Removal of the pistol-shaped visual obturator and laparoscope from the introduced trocar. The obturator is taken off of the laparoscope, which is then reinserted into the port for initial inspection.

#### *Open transperitoneal access*

In cases where standard insertion of an insufflating needle or closed trocar insertion is associated with a significant risk of injury to underlying structures, it may be preferable to perform an open access to the peritoneal cavity. This is often utilized in patients who have had significant prior transperitoneal surgery raising concerns about adhesion formation. Adhesions of omentum, bowel, bowel mesentery, and in some cases solid organs such as the liver to the anterior abdominal wall prevent these structures from falling away from the parietal peritoneum as it is elevated during insertion of the needle or following insufflation. This can result in direct puncture or laceration injuries of these structures with either the Veress needle or the initial trocar. These injuries can even occur utilizing direct vision trocars since it can be difficult to discern the passage of one of

these devices into or through adhered viscera from passage through the preperitoneal layer.

In these circumstances, it is often prudent to use an open access to establish the pneumoperitoneum. This technique is performed by making a 1.5–2 cm incision at the site of desired trocar insertion. The underlying fascia is exposed using deep, narrow retractors and incised. Stay sutures of 0-Vicryl (polyglactin) mounted on a semicircular needle are inserted through the corners of the fascial incision. The underlying muscle fibers are split using a tapered clamp and the posterior fascial layer is incised. The preperitoneal fat is grasped and gentle spreading motions of the Metzenbaum scissors reveal the underlying peritoneal layer. The peritoneum is tented up between grasping, nontoothed forceps and cut (Figure 10.4). Entry into the peritoneum is confirmed by visualization of freely mobile bowel or omentum. A blunt-tipped



**Figure 10.3** (A) Visiport device (USSC, Norwalk, Connecticut) with its cutting blade that is activated each time the trigger is depressed. (B) Removal of the visual obturator and laparoscope from the introduced port.

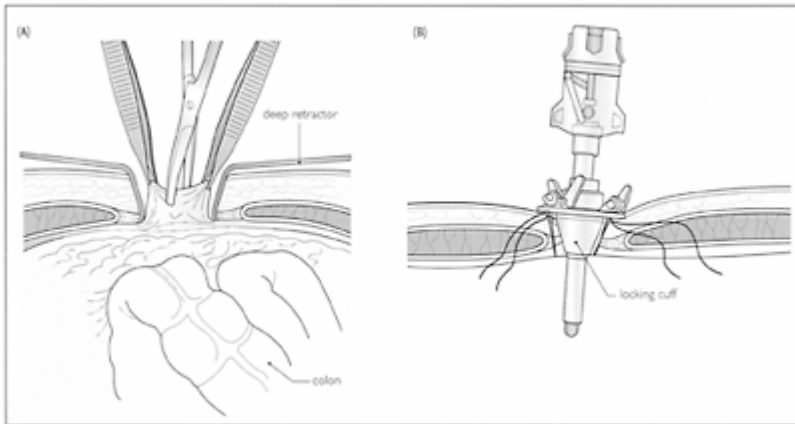
cannula, such as a Hasson, is inserted through the opening in the peritoneum. The fascial corner stitches are wrapped around the circular suture guides holding the Hasson trocar in

place. The cuff is then pushed into the skin incision and locked into position to prevent leakage of the pneumoperitoneum (see Figure 10.4).

One drawback of the open access technique is the larger skin incision required for introduction of the initial cannula than what is necessary using a closed introduction. In addition, a larger fascial incision than the diameter of the port is often made and can result in problematic leakage of the pneumoperitoneum around the cuff of the Hasson cannula. Overall, this approach takes longer to perform than the closed technique and can be extremely difficult in obese patients due to the thickness of the subcutaneous and preperitoneal fat layers.

### *Hand-assisted access*

Early-generation hand-assist devices such as the Pneumo Sleeve (Week Closure Systems, Research Triangle Park, North Carolina) relied on applied or tape-backed adhesives to secure the device to the skin of the abdominal wall. This required initial insufflation and distention of the abdomen to allow smooth application of the device and to prevent leakage and detachment on creation of the pneumoperitoneum.<sup>3</sup> The latest generation of devices relies on inner and outer abdominal securing rings attached by a wound protector. The pneumoperitoneum is then maintained around the inserted hand via an occlusive gel matrix (GelPort; Applied Medical, Rancho Santo Margarita, California), twisted pneumatic cuff (OmniPort; Week Closure Systems, Research Triangle Park, North Carolina),

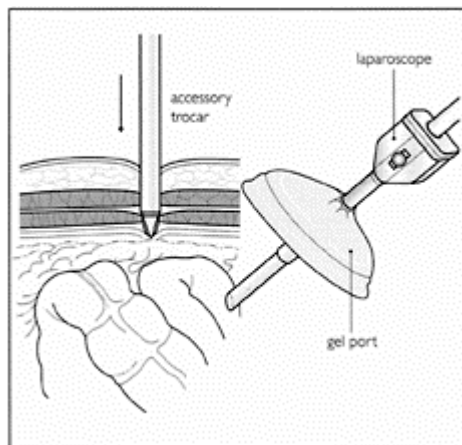


**Figure 10.4** (A) Incision of the peritoneum being made for open access port introduction. (B) Insertion of the Hasson port and securing of the locking cuff to prevent leakage of the pneumoperitoneum using the

previously placed fascial corner stitches.

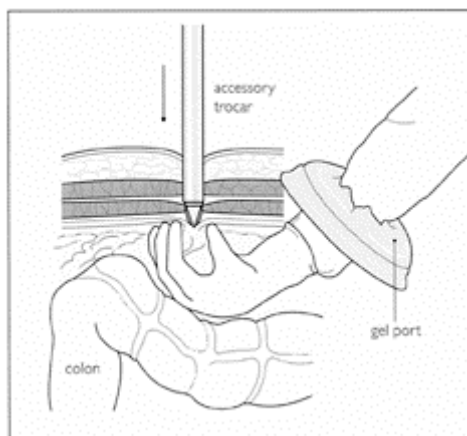
or an adjustable iris (Lap Disc; Ethicon Endo-Surgery, Cincinnati, Ohio). With each of these new generation of devices, the incision for the hand-assist port can be made first and the secondary ports inserted under direct inspection or with the aid of an inserted hand in a nonvisualized fashion.

In the method utilizing direct inspection, a 10/12 mm port is inserted via the hand device through the gel matrix (GelPort), aperture of the twisted pneumatic cuff (OmniPort), or adjustable iris (Lap Disc). These devices can be secured around the inserted port in identical fashion to the operating hand and the abdomen insufflated to allow for insertion of the additional trocars under direct vision (Figure 10.5). An alternative to direct inspection is to place the laparoscopic ports with the aid of the inserted hand. The hand is cupped beneath the point of entry of the trocar, palpated as an area of downward-tented peritoneum and transversalis fascia. The inserted hand acts as a backstop to the abdominal wall and shields the peritoneal contents from the entering trocar (Figure 10.6). Non-bladed trocars should be utilized in this method to avoid injury to the surgeon's hand. If any adhesions are felt, it is best to take them down first under direct inspection through the hand-assist port incision prior to inserting additional trocars.



**Figure 10.5** A trocar has been inserted through the gel matrix of the GelPort hand-assist device (Applied Medical, Rancho Santo Margarita, California) and direct visual confirmation is being performed of an accessory port as it is introduced into the abdomen.





**Figure 10.6** Secondary port placement is being performed with the surgeon's hand inserted via the hand-assist device, protecting the abdominal contents as a nonbladed trocar is introduced into the peritoneal cavity.

#### *Closed retroperitoneal access*

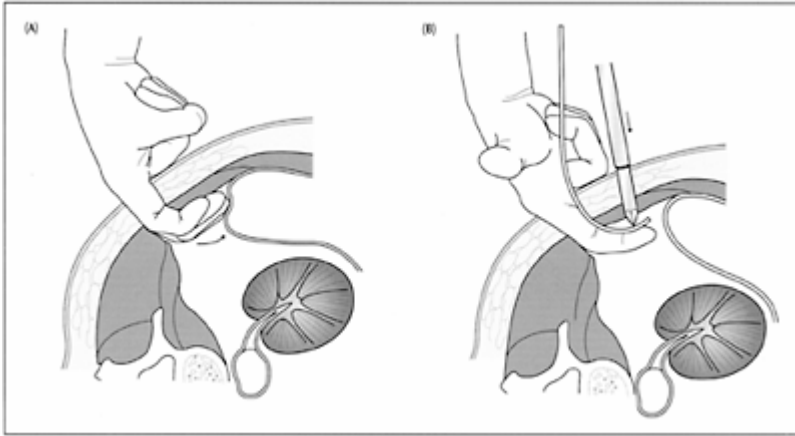
Depending upon individual surgeon preference or clinical situations in which peritoneal exposure may be limited, access to the retroperitoneum may be desired. Closed access can be obtained via direct retroperitoneal insufflation in the flank position using a Veress needle inserted at the posterior axillary line midway between the 12th rib and the iliac crest. After establishing the pneumoretroperitoneum, a visual or standard cannula can be introduced. An alternative access option is the introduction of a direct vision trocar such as the Optiview or Visiport at the same location without prior insufflation. Regardless of the closed technique utilized, care must be exercised to insert either the needle or direct vision trocar at an angle approximately  $10^\circ$  anterior from vertical.<sup>4</sup> This degree of angulation helps to avoid entry into the psoas and quadratus muscle posteriorly and the bowel and peritoneum anteriorly. Introduction of a visual cannula into the retroperitoneum is performed in exactly the same fashion as it is for transperitoneal surgery; however, the final layer of entry is into the retroperitoneal fat as the cannula traverses the inner muscular fascia. Once this layer is entered, the insufflant is attached and gentle blunt dissection is then performed with the laparoscope to generate adequate space for additional trocars. It is important to sweep the peritoneal envelope medially to prevent transperitoneal placement of the accessory ports, which can result in loss of retroperitoneal distention or inadvertent visceral injury.

*Open retroperitoneal/extravesical access*

To avoid the risk of colonic injury, open retroperitoneal access is often preferred. In this approach, a several-centimeter incision is made off of the tip of the 12th rib and carried down through the underlying fascia. The muscle fibers are then split along their course using deep, narrow retractors and the retroperitoneum is entered using a tapered clamp. Once the retroperitoneal fat is identified, a finger is inserted via the incision and used to perform blunt dissection to create space for a retroperitoneal dilating balloon. There are several commercially available dilating balloons (e.g. Origin Medsystems, Menlo Park, California) that allow dilation either with or without direct vision. Correct cephalad placement behind Gerota's fascia is critical to maximize the beneficial impact of the balloon on creation of the retroperitoneal space. An alternative and more cost-effective method of balloon dilation utilizes a finger cut from an operative glove and secured to a 16F red rubber catheter with a 2-0 silk suture. The 'finger balloon' is then sequentially inflated using a catheter tip syringe with clamping after each instillation until a total volume of 500 ml of saline is instilled. Once dilation has been performed and the desufflated balloon removed, the surgeon can insert his finger into the retroperitoneum to further sweep the peritoneum medially. Additional trocars can then be introduced directly onto the palpating finger, which is protected using a narrow malleable retractor (Figure 10.7), or under direct vision once the pneumoretroperitoneum has been established.<sup>5</sup>

*Potential pitfalls of accessing the abdomen***Vascular injury**

Access-related injuries to the aorta, vena cava, iliac, and epigastric vessels occur in approximately 0.25% of cases.<sup>1</sup> The risk of such injuries can be reduced by using direct vision, open access, or hand-assist techniques for introduction of the initial port. Confirmation of vascular injury is usually the prompt return of a significant quantity of blood via the inserted Veress needle or trocar. Delayed recognition of a major vascular injury until introduction of the laparoscope demonstrates the presence of brisk intraperitoneal or retroperitoneal bleeding is also possible. In such cases the access needle port punctures or lacerates a major vessel prior to being repositioned. Vascular trauma that occurs during establishment of the initial access is often difficult to manage laparoscopically since an adequate number of working ports have not been introduced and the time required for insertion and control is



**Figure 10.7** (A) Secondary port placement during open retroperitoneal access can be performed after manually sweeping the peritoneal envelope medially off of the abdominal wall. (B) The accessory port is then introduced directly onto the palpating finger, which can be protected with a malleable retractor or use of a nonbladed trocar

often prohibitive. In the case of such large-vessel entry access injuries, prompt open conversion is usually necessary to avoid catastrophic blood loss.

Venous gas embolism can also occur if insufflation is attempted while the Veress needle is inserted into a large vein. The reported incidence of clinically detectable venous gas embolism is 0.002–0.08% and presents clinically as facial plethora, jugular venous distention, inability to oxygenate, and cardiovascular collapse.<sup>6</sup> A classic mill-wheel murmur is auscultated over the heart and right-heart strain is evidenced on the electrocardiogram. Prompt release of the pneumoperitoneum, head-down with right-side-up positioning, and 100% oxygen administration are critical steps toward reversing this life-threatening situation.<sup>6</sup>

### Bowel injury

Inadvertent injury to the bowel during laparoscopy occurs in approximately 0.13% of cases, 32% of which happen during Veress needle or trocar insertion.<sup>7</sup> Selecting an entry point furthest away from areas of scar tissue minimizes the potential for injury. In the flank position, it is often preferable to insert the needle in the lower quadrant of the upside, since the small bowel tends to be displaced medially and injury to the colon, or

solid viscera, will be less likely than it would with insertion in the midline or upper quadrant. Entry into the bowel may be suspected if uneven insufflation of the abdomen is noted, or verified on aspiration of succus entericus or fecal contents. In these cases, leaving the needle in place and performing an open access technique is recommended. If the needle is identified entering the bowel via an isolated puncture site, this can usually be laparoscopically oversewn. Lacerations or thermal injuries of the bowel must be repaired meticulously via the laparoscope or converted to an open exposure if necessary to confirm the quality of the repair. If the needle is not found entering the bowel on initial inspection via the open access, but an injury is still suspected, then the bowel should be run and any suspicious areas oversewn.

It is important to recognize the presenting signs of occult bowel injury following laparoscopy because 70% of these injuries will go unrecognized during the laparoscopic case.<sup>7</sup> Some of the more common presenting signs include focal trocar site pain, leukopenia, and diarrhea.<sup>7</sup> Abdominal-pelvic computed tomography (CT) has been shown to assist in the diagnosis of bowel injuries.<sup>8</sup> Early recognition and intervention is important, as profound sepsis with cardiovascular collapse and death can occur.<sup>7</sup>

### **Preperitoneal insufflation**

Insufflation between the abdominal wall musculature and the peritoneum is usually recognized by a rapid early rise in insufflation pressures. The total volume of infused gas is markedly reduced from what is observed during intraperitoneal insufflation, although it can still be substantial in larger patients. Unfortunately, this condition may not be recognized until introduction of the initial port, when inspection reveals web-like attachments and the confining peritoneum preventing visualization of the bowel. A non-bladed visual cannula can be utilized to advance the lens through this space and into the peritoneal cavity, which is initially collapsed due to the intervening preperitoneal insufflant. The extent of the separation can, however, make this maneuver difficult due to compression of the peritoneal sac and the resultant proximity of the underlying bowel. Once the peritoneum is entered and the line of Toldt is incised, the space rapidly equilibrates. The expansion of introduced gas tracking from the preperitoneal space can actually facilitate the retroperitoneal dissection in some cases.

### **Omental insufflation**

Insertion of the Veress needle into the omentum is usually heralded by intermittent elevations of the intraperitoneal pressures that improve periodically with minor adjustments of the depth of needle penetration. Upon insertion of the initial trocar, a diffuse bubbled appearance of the omentum is noted. The primary detriment of this condition is the negative impact it can have on visualization, which is usually minimal, and the possibility of lacerating an omental vessel.

## **Trocar placement**

The specific trocar arrangements utilized for each operation will be given in their corresponding chapters. These remain a rough guideline that can be altered depending upon the specifics of patient habitus, individualized pathology, instrument preference, and surgeon hand dominance. However, several general principles should be recognized and are outlined in this section.

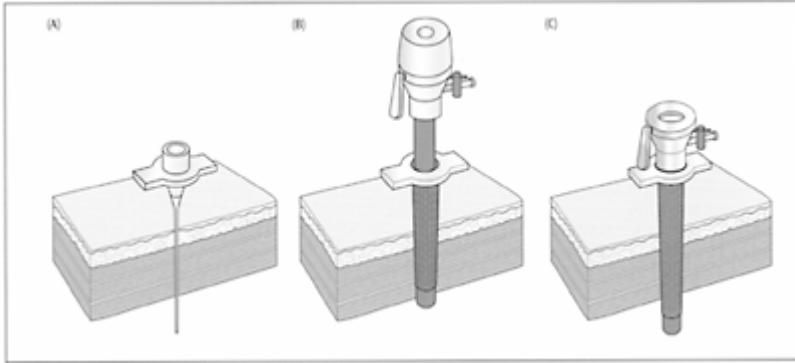
### *Trocar introduction*

Controlled insertion of laparoscopic trocars of any type is best accomplished by making an epidermal and dermal incision slightly larger than the trocar itself. This prevents 'gripping' of the trocar on introduction that can lead to compression of the abdominal wall and peritoneal envelope with subsequent injury to the underlying viscera or vasculature. An adequate-size incision also prevents excessive pressure at the trocar skin edges during the operation, which can result in tissue necrosis, cellulitis, and larger areas of scarring. The underlying fat is spread down to the level of the fascia using a narrow-tipped clamp. Two-handed introduction of the trocar with the non-dominant hand positioned on the shaft of the trocar, controlling the speed of entry, prevents excessively rapid introduction of accessory ports. An alternative single-handed introduction, with the index finger of the dominant hand extended along the shaft of the trocar to limit the extent of entry, can also be utilized. All ports should be inserted with slight angulation toward the surgical organ of interest. This insures that the anterior and posterior fascial incisions do not line up, thereby reducing the risk of hernia formation. A more perpendicular introduction of the port can also limit excursion toward the surgical organ of interest, causing unnecessary resistance during the dissection.

There are three main types of trocars available on the market: fascial-cutting, fascial-splitting, and radial-dilating trocars. Once initial access has been obtained, these additional ports should always be inserted under direct visual inspection by the laparoscope. Fascial-cutting trocars have an internal obturator with either a mounted pyramidal or single blade that cuts the fascia as it is advanced through it. Once the insufflated peritoneum is entered, the blade retracts within a protective obturator. The port is then advanced until the insufflation side hole is visualized within the peritoneal cavity. It is often best to place a securing suture around the side port of fascial-incising trocars to prevent dislodgment, since there is less resistance to withdrawal during instrument exchanges. The securing suture is tied at the skin level using an air-knot; each end is then wrapped around the side port proximal to the stopcock, and tied again.

Fascial-splitting trocars require slightly more force to insert than the bladed trocars and are advanced using a back-and-forth twisting motion. Once the fibers of the fascia begin to split, it is important not to release applied pressure to the trocar to prevent the obturator tip from backing out of the fascia and creating a separate fascial opening. The fascia tends to grip these ports more vigorously than the bladed trocars and securing sutures to prevent dislodgment of the port are often unnecessary. Radial-dilating ports (Step System; Week Closure Systems, Research Triangle Park, North Carolina) also split

the fascia, but provide the additional option of increasing the size of the inserted trocar from 5 to 12 mm using a series of stepwise ports with their dilating obturators inserted into a mesh-like sheath. This enables the operating surgeon to minimize port size and enlarge a specific access at any time during a case when necessary (Figure 10.8).



**Figure 10.8** (A) The mesh-like expandable sleeve of the Step Access System (Week Closure Systems, Research Triangle Park, North Carolina) is introduced into the peritoneal cavity over an insufflation needle. (B) The needle is removed and radial dilation is performed to the desired size using a blunt tip obturator and cannula inserted via the mesh sheath. (C) The obturator is removed and the port is ready for use.

#### *Size selection*

Port sizes include 2 mm ‘needlescopic’, 5 mm, 10/12 mm, and 15 mm sizes. Choosing the size of the trocar depends upon the equipment that will be inserted via the specific port. Therefore, each port must be large enough to accommodate the diameter of the largest instrument that will potentially pass through it. For example, one of the largest frequently used pieces of equipment is the Endovascular linear stapling device, which requires a 12 mm port, so a 10/12 mm port should be utilized at all sites where it may be introduced. An alternative to starting with the largest anticipated diameter is to utilize a radial-dilating trocar (e.g. Step System). The mesh-like sleeve allows rapid dilation of the access via a single fascial incision if the port requires upsizing for insertion of a larger instrument than initially anticipated. Separate snap-on flap ‘toilet seat’ reducers or universal reducer seals allow use of 5 and 10 mm instrumentation via 10/12 mm ports

and Versaports (USSC, Norwalk, Connecticut) are produced with universal adapting seals. It is always desirable to utilize the smallest trocars possible to minimize the morbidity of the fascial and muscular puncture and to limit the number of port sites requiring fascial closure. In adult patients, it is not necessary to close 5 mm port sites; however, these should be closed in children due to the risk of omental herniation. Instruments requiring more controlled movements such as the Endovascular stapling or EndoStitch device (AutoSuture, Norwalk, Connecticut) are preferably manipulated using the surgeon's dominant hand at an acceptable angle for application, which dictates location of the appropriate trocar size.

### *Trocar length*

A standard trocar length of 75 mm in pediatric and 100 mm in adult patients of average size adequately penetrates the abdominal wall and provides stable access to the abdominal cavity. In some morbidly obese patients, extra long trocars measuring 120 mm may be required to prevent the trocar from backing out of the peritoneum, which can be time consuming to reintroduce and lead to subcutaneous emphysema. The abdominal pannus is a mobile structure in obese patients and is often hanging medial and inferior to the corresponding fascial entry point for patients in the flank position. More cephalad and lateral introduction of the ports is required in these patients for proper access to retroperitoneal organs when approached in a transperitoneal fashion.<sup>9</sup> This also avoids the excess thickness of the subcutaneous fat contained within the abdominal pannus.

### *Potential pitfalls of trocar placement*

#### **Inadequate trocar spacing**

In general, ports should be placed a distance apart corresponding approximately to that between the index and little finger to limit crossing instruments or so-called sword fighting. Instruments may still cross with extreme movements, even with the widest separation of the port sites. Utilizing an angled lens can minimize these interactions, if they are due to the laparoscope. If interactions are due to the instrument of an assistant, the offending device can usually be inserted via a different port site, which results in less interference. Other elements the surgeon should always be aware of when planning port placement include osseous barriers such as the ribs, pelvis, or spine and the edge of any inserted hand-assist device. All of these structures can inhibit deflection of the instruments. The amount of separation required from these areas is fairly minimal when they are close to the fulcrum point of the port. Downward and lateral deflection of instruments should also be inspected prior to insertion of the ports to avoid inadequate tip movements due to contact with the table, padding, or extremities.

#### **Mirror imaging**

Any time the angle created between the inserted laparoscope and the operating instrument exceeds 90°, mirror imaging occurs in the primary tower, leading to counterintuitive movements. In general, positioning the camera port between the operating surgeon's two

working ports is preferable. However, as long as the laparoscope is inserted within a 90° array of the two introduced working instruments, the procedure can usually be performed without difficulties due to mirror imaging. It is important to take into consideration the extent of the dissection and to have an appropriate plan for shifting the position of the laparoscope if necessary to avoid counter-intuitive movements. If possible, it is also best to limit the amount of mirror imaging experienced by the assistant surgeon in the secondary tower to expediate the flow of the operation.

## **Exiting the abdomen**

### *Final inspection*

Once the laparoscopic operation has been completed, the areas of the dissection should be thoroughly inspected for any signs of bleeding or occult visceral injury. If questionable biliary or pancreatic injuries are present, a drain may be required for adequate monitoring and drainage. All serosal bowel injuries should be repaired either laparoscopically or via an extended port incision as these can ultimately lead to perforation and fistulization, especially when they are a result of thermal injury.<sup>7</sup>

Once the surrounding structures are determined to be free of injury and hemostasis is deemed adequate, all dissection sites should be reinspected under low insufflation pressures of 5 mmHg pressure. Higher intraperitoneal pressures can tamponade regions of venous bleeding resulting in unnecessary post-insufflation blood loss and possible hematoma formation. Hemostasis of any observed areas of bleeding can then be obtained using the harmonic shears, electrocautery, direct pressure with surgical cellulose (Surgicel, Johnson & Johnson, Inc., Arlington, Texas), hemoclips, laparoscopic suturing, fibrin glue, or other techniques.<sup>10</sup> The entry point of each trocar should also be inspected for bleeding on removal and insertion of the port closure sutures. If vigorous abdominal wall bleeding is noted from any of these sites, it may require placement of a figure-of-eight suture rather than a simple closure stitch, especially in cases of inferior epigastric vessel injury.

### *Fascial port closure*

There are several options available for closure of laparoscopic port sites. In patients with minimal amounts of subcutaneous fat, one option is direct vision closure. This is accomplished using narrow, deep retractors such as the Army-Navy retractors to expose the underlying fascia. Sutures of 0-Vicryl mounted on a semicircular needle are then passed through the cut edges of the fascia, which are then tied together to complete the closure. Subfascial herniations at laparoscopic port sites have been reported, indicating the benefit of including the peritoneal layer in the closure.<sup>11</sup> The peritoneum is not incorporated when a direct vision closure is performed in an adult patient, thereby increasing the risk of this type of herniation.

A more reliable method of closing the port site utilizes a suture-grasping needle such as the Carter-Thomason device (Inlet Medical Inc., Eden Prairie, Minnesota), which includes both the fascia and peritoneum in the closure.<sup>12</sup> One effective technique for

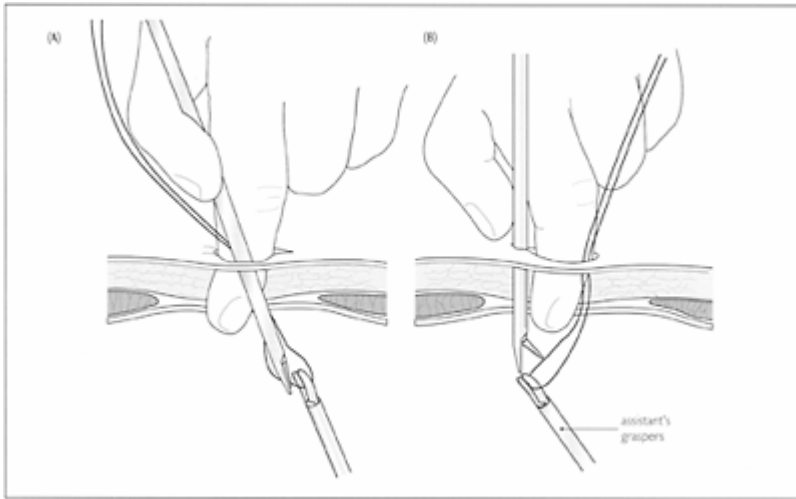


obtaining a good fascial closure using the Carter-Thomason device involves removal of the port and insertion of the index finger of the non-dominant hand into the defect. This prevents release of the pneumoperitoneum and allows the surgeon to feel the cut edges of the fascia. The thumb and first two fingers of the dominant hand are inserted into the handle of the device. As the thumb is drawn back in the spring-loaded handle, the jaw opens. The thumb is then squeezed toward the index and middle fingers to close the jaws, which squeeze together to grasp a 0-Vicryl suture approximately 1 cm back from its end.

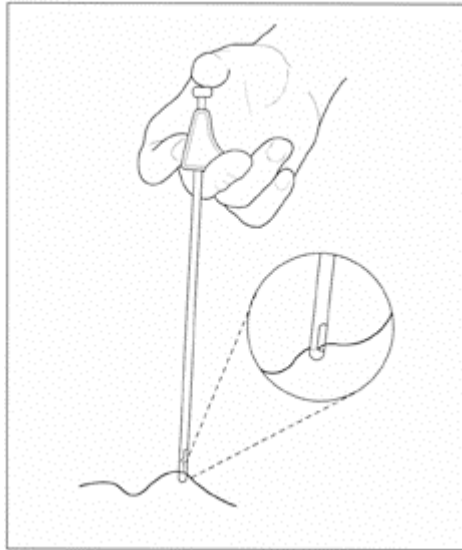
The grasping needle is inserted below the skin level and through the center portion of the fascial edge until it can be visualized with the laparoscope entering the intraperitoneal space. The speed of entry is controlled by pinching the shaft of the needle between the side of the inserted index finger and the pad of the thumb (Figure 10.9). It is critical to maintain direct vision of the tip of the Carter-Thomason needle as it enters the peritoneum to avoid inadvertent injury to the bowel, solid viscera, or vasculature. The grasping needle is advanced for a distance of 1–2 cm into the peritoneal cavity and is then withdrawn slightly to create slack in the introduced loop of suture. The assistant uses a grasper to grab a portion of the suture within the peritoneal cavity. The handles of the closure device are separated to open the jaws of the grasping needle, which releases the suture as the assistant pulls it from the jaws of the device. The jaws of the Carter-Thomason device are then closed and it is withdrawn. The grasping needle is then reinserted through the fascia on the opposite side of the incision and into the peritoneal cavity. The jaws of the Carter-Thomason device are once again opened, the suture is passed into the jaws, and the end is pulled out through the fascia, completing placement of the simple closure stitch (see Figure 10.9). If the surgeon does not wish to insert the grasping needle adjacent to his finger, a conical guide with side holes can be utilized or the needle can simply be passed along either side of the port itself.

When a laceration of an abdominal wall vessel occurs at the site of port closure, or a wide gap in the fascial defect exists, the Carter-Thomason device can also be utilized to place a figure-of-eight instead of a simple stitch. Once passage of the suture is complete, the trocar is then reinserted using the blunt obturator and the stitch is tagged until a similar closure suture has been placed at each of the other port sites.

An alternative needle closure device is the EndoClose (AutoSuture, Norwalk, Connecticut), which functions similar to the Carter-Thomason needle but relies on a retractable hook on the internal obturator of the needle to grasp the suture. As the thumb of the dominant hand pushes down on a spring-loaded button on the handle of the device, the obturator advances, releasing the hooked suture, which is then grasped by the assistant. The needle is reinserted through the cut fascia of the opposite side and the button is depressed to once again expose the hook. The suture is wrapped around the needle and slid into the crotch of the hook. As the button is released, the hooked



**Figure 10.9** (A) The Carter-Thomason closure device (Inlet Medical Inc., Eden Prairie, Minnesota) introduces a 0-Vicryl suture through one of the fascial edges, which is then grasped by an assistant. (B) The grasping needle is reinserted through the opposite fascial edge and the assistant transfers the suture back into the jaws of the device, which is then withdrawn to complete the stitch.

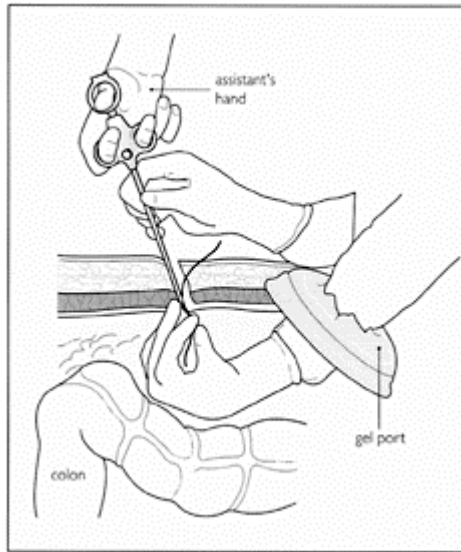


**Figure 10.10** The EndoClose (AutoSuture, Norwalk, Connecticut) fascial-suturing needle functions in similar fashion to the Carter-Thomason device, but utilizes a retractable hook instead of grasping jaws to secure and transfer the suture through the fascial edges.

suture is pulled tight against the edge of the needle by the retracted obturator and the suture is drawn out through the fascia to complete the stitch (Figure 10.10).

#### *Closing the hand-assist port and accessory ports*

If a hand-assist port is utilized, the inserted hand is used to grasp the suture and to perform the exchanges between the jaws of the Carter-Thomason or EndoClose device, much like the grasping instrument was utilized during port closure on the standard laparoscopic cases. To control entry of the fascial closure device, the assistant squeezes the handle of the grasper, keeping the jaws closed on the suture, while the operating surgeon advances the grasping needle through the fascia. The inserted hand can be cupped beneath the area of the fascial defect, with the middle finger inserted into the defect to prevent escape of the pneumoperitoneum. Care must be taken to prevent inadvertent injury to the inserted hand. Once the suture enters the abdomen, it is grasped between the thumb and forefinger of the inserted hand and is drawn in further to



**Figure 10.11** Fascial closure being performed using the Carter-Thomason device and a hand inserted via the hand-assist port. The surgical assistant manipulates the handle of the Carter-Thomason device as the primary surgeon grasps the shaft of the needle and controls the speed and location of its insertion. The introduced hand acts like the grasper during a standard laparoscopic closure and performs the suture transfer into and out of the jaws of the fascial closure device.

facilitate passage to the jaws of the closure device after it has been inserted through the other side of the fascia (Figure 10.11). The trocars are reinserted, as outlined previously, until all closure sutures have been placed, and are then tied down with the inserted hand separating the peritoneal organs from the abdominal wall to prevent entrapment.

#### *Desufflation of the abdomen*

The 5 mm trocar sites should be removed prior to tying the fascial closure sutures of the 10/12 mm ports. This allows potential placement of a closure stitch at these sites, while the 10/12 mm ports can still be utilized should port-site bleeding occur. Each of the 10/12 mm ports are removed under visual inspection, leaving the umbilical port (supine case) or

the lower quadrant port (flank case) until the end. Once all of the other fascial closure sutures have been tied down, the insufflant is shut off and the side port of the remaining trocar is opened. The patient is positioned so the final exit port is elevated and the laparoscope is directed into all remaining areas of the pneumoperitoneum as a hand is used to compress the abdominal wall, assisting in evacuation of the insufflant. The anesthesiologist is instructed to give the patient several large extended breaths to help in expulsion of any areas of collected pneumoperitoneum beneath the diaphragm. Once desufflation appears complete, the fascial closure suture of the one remaining port is elevated and the trocar is slid out, leaving the laparoscopic lens in place within the peritoneal cavity. The lens is slowly withdrawn in a vertical orientation, taking care to observe the peritoneal contents falling back into the abdominal cavity as the laparoscope passes out through the muscular fascia.

For hand-assisted laparoscopic procedures, desufflation can be performed quite effectively via the hand-assist incision. The omentum should be used to cover the underlying viscera in the base of the incision whenever possible to prevent adhesion formation and reduce the risk of bowel entrapment. The hand-assist incision is then closed using a running #1 polydioxanone surgical (PDS) suture in patients with healthy fascia. If wound healing comorbidities exist, such as steroid use, diabetes, or obesity, interrupted figure-of-eight nonabsorbable permanent sutures should be utilized.

The skin incisions are irrigated with an antibiotic solution and injected with 0.25% bupivacaine. Several interrupted 3–0 Vicryl dermal sutures are placed for hand-assist or organ extraction incisions followed by a running absorbable subcuticular suture and Steri-strips. Band-Aids or small folded gauze dressings are placed at trocar sites and an adhesive island dressing is applied to the hand-assist or organ extraction site.

### *Potential pitfalls of exiting the abdomen*

#### **Inadequate desufflation and shoulder pain**

Carbon dioxide insufflant is a peritoneal irritant and residual collections beneath the diaphragm can irritate the muscle, causing referred pain to the region of the shoulder, scapular muscles, and trapezius. Once this condition occurs, the patient can be quite uncomfortable and must await eventual resorption of the pneumoperitoneum. Prevention via careful and complete release of all insufflant is paramount. Methods to reduce the discomfort include periods of supine or head-down positioning to displace the carbon dioxide to regions of the peritoneum away from the diaphragm. Anti-inflammatory pain medication and warm shoulder packs can also provide varying degrees of relief.

#### **Bowel or omental herniation**

The incidence of port-site herniation is approximately 1% in most published series and is usually due to a poor fascial closure, but it can result from associated factors such as localized infection, diabetes, coughing, or steroid use.<sup>2,13</sup> Trocar sites where the fascial incision is extended for specimen extraction are also at higher risk for herniation, possibly due to fascial attenuation that can occur from torquing the laparoscopic ports during the procedure and on removal of the specimen.<sup>13</sup> At port sites through which

specimen morcellation is performed, it is advisable to place a figure-of-eight or several interrupted sutures as additional tension and stretching of fascial fibers often occurs during the fragmentation process. It has been suggested in the literature and by the manufacturers of fascial-splitting trocars that it is not necessary to close the fascial defects created by these ports due to their low risk of herniation.<sup>2</sup> A case of herniation following use of one of these trocars in a donor nephrectomy patient has recently been reported.<sup>14</sup> As a result, we now recommend closure of the fascia for all 10/12 mm port types.

In pediatric patients, closure of 5 mm ports is also recommended, due to the potential for omental herniation. These ports can usually be closed via the skin incision under direct vision, due to the limited amount of subcutaneous fat in pediatric patients, although fascial closure devices may be more efficient in larger or older children. Presenting signs of port-site herniation vary depending upon the timing of the occurrence and the presence or absence of bowel ischemia. On occasion, evidence of asymptomatic herniation may be found incidentally during follow-up imaging studies or physical examination. Patients can also present with more subtle signs of intermittent bowel obstruction or, at the other end of the spectrum, with severe acute obstruction manifested by abdominal distention, nausea, and vomiting. If the prolapsed portion of bowel becomes ischemic, focal trocar site pain, diffuse abdominal pain, and eventually signs of bowel necrosis, abdominal wall cellulitis, peritonitis, and sepsis can ensue.

In the acute setting, it may be possible to manage a herniation via laparoscopic reduction. Open exploration, however, is preferable in the acutely ill patient in whom complete bowel inspection and potential resection is required.

### **Abdominal wall vessel bleeding**

Epigastric or abdominal wall vessel lacerations may not become evident until the trocars are removed at the end of the case, since the port can tamponade the point of injury. Placement of a figure-of-eight suture around the bleeding vessel using a grasping needle such as the Carter-Thomason device can be used to obtain hemostasis, which is then confirmed under direct visual inspection. Other methods, such as the use of electrocautery or an inserted Foley catheter whose balloon is inflated and pulled tight against the bleeding point, have also been utilized.<sup>10</sup> On occasion, open exposure and ligation of the lacerated vessel is required. Lack of early recognition of this condition can lead to significant blood loss and large rectus or abdominal wall hematoma formation.

### **Conclusions**

Careful access entry, trocar placement, and exiting the peritoneum or retroperitoneum are critical elements of any laparoscopic operation. These steps require the same degree of forethought and careful execution as the procedure itself to insure success of the operation and avoid potential complications.

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# 11

## Laparoscopic training—basic to complex skills

Debora K Moore and Robert G Moore

Over 200 articles have been written dealing with laparoscopic training models, but few are related to urology. In fact, in the last 8 years, <20 articles have been written pertaining to educational aspects of training laparoscopic urological skills!<sup>1-13</sup>

### Educational principles

To improve our ability as surgical educators, it is helpful to review studies in adult learning theory and the acquisition of technical skills. Research on the acquisition of surgical technical skill has traditionally adopted a theory described by Kopta.<sup>14</sup> He defined three phases of learning a skill starting with cognitive learning, progressing to integration of knowledge with appropriate motor behavior, and, finally, a phase is reached in which performance is smooth, automatic, and resistant to stress.<sup>15</sup> Later studies question the notion of automaticity. Apparent automaticity observed in expert performance is believed to actually reflect development of a complex cognitive network. This complex network facilitates improved prediction, awareness, and cognitive representation of tasks.<sup>16</sup>

Using the principles of 'learning hierarchies', a concept at the heart of the behaviorist school of thought, an individual must learn basic component skills of a routine before progressing to the full routine ('chunking').<sup>17</sup> More simply put, one breaks a complex task into simple components and then integrates them after successfully mastering each component.

Cognitive theories support the idea that repetitive practice facilitates the subsequent performance of motor activities by permitting more efficient interpretation of proprioceptive, visual, and tactile feedback.<sup>18</sup> Neurophysiologic testing has further illuminated the value of a prior perceptual framework. These are standardized instruments that measure specific components of motor skills, including pure motor ability, imagery, and visuospatial orientation. Schueneman et al conducted neurophysiologic tests on surgical residents, correlating results with faculty ratings of their surgical skill.<sup>19</sup> They found no correlation between surgical skill and pure motor abilities such as speed and precision. Instead, surgical skill ratings correlated with a complex of activities, including but not limited to visuospatial organization, somatosensory memory, and stress tolerance. 'Visuospatial perceptual skill' is the ability to use landmarks to create a mental picture of relationships in three-dimensional space. 'Somatosensory memory' is the ability to interpret sensory cues based on prior



experience. 'Stress tolerance' is the ability to distinguish essential detail from nonessential detail.<sup>20</sup>

Shadmehr and Holcomb looked at neural correlates of motor memory consolidation. They monitored changes in cerebral blood flow, an indirect marker of neural activity, using positron emission tomography to study the acquisition of newly learned motor skills. They concluded that it takes 4–6 hours for the memory of new skills to shift from prefrontal regions of the cortex, a temporary storage site, to the premotor, posterior parietal, and cerebellar cortex structures, which represent permanent storage. Using this information, they felt that allowing for this time passage before teaching a new motor skill should increase functional stability of the previously learned skills.<sup>21</sup>

Current educational theories emphasize the importance of incorporating cognitive learning side by side with skill practice and drills. Frequent feedback is essential and must incorporate both cognitive and technical elements.<sup>22</sup> Lastly, it has been well documented that adult learning is enhanced by a self-directed approach centered on the learner not the teacher, with specific goals identified and in which continued constructive feedback is given.<sup>23</sup>

Using these concepts to train surgeons in laparoscopic surgery requires a program that allows the trainee to enhance proprioceptive and tactile perceptions while developing visuospatial orientation through an operative video camera. Once mastered, this foundation can be used to develop perceptual experience with more difficult surgical skills. Frequent and repetitive practice appears to be important to retention of these skills. If somatosensory memory not pure motor ability is important, tissue models that closely resemble true surgical tissues would be valuable. Improving perceptual skills, providing a thorough knowledge of laparoscopic equipment, including their capabilities and limitations, and adherence to surgical principles, enhances stress tolerance. Finally, in order for an education program to be effective it should honor the principles of adult education, allowing for self-directed learning and continued feedback.

### **Problems specific to laparoscopic training**

Training residents to operate has traditionally been done in the operating room using a system introduced by Halsted more than a century ago.<sup>24,25</sup>

Customarily, open surgical skills have been acquired by hands-on experience, allowing tactile sensation and direct vision of the tissue under the guidance of an experienced surgeon. Minimally invasive surgery presents significant and unique challenges to the traditional modes of training that need to be addressed in order for it to be performed in a quality fashion.<sup>26</sup>

The first challenge to overcome is working in a three-dimensional field off a two-dimensional image monitor: in simple terms, the operator loses depth perception. Studies have shown that the mind will not accept the lack of depth perception on the video monitor and will subconsciously project depth.<sup>27,28</sup> To compensate for loss in depth perception, visual cues are used to aid in position determination.<sup>29</sup> Motion parallax, the motion of an instrument past the camera while it remains in a fixed position, angulation, the angle of the instruments when introduced into the visual field, and known reference points, all contribute to the estimation of depth on a flat screen. Touching an object in the

visual field creates a known reference point and this mentally aids in depth perception during laparoscopic procedures.

Another difficulty encountered in learning to perform laparoscopic surgical skills is that the current trocars and instruments used have restricted degrees of operative movement and many deny any wrist or elbow motion. This problem of restricted degrees of freedom is compounded by the fulcrum or lever effect currently inherent in laparoscopic surgery. Because the trocar, through which the instrument passes, is fixed in the abdominal wall, an upward movement of the instrument handle causes a downward displacement of the end effectors and vice versa. To minimize this restriction, trocar and camera positions should be optimized; ideal positions have been determined by the experts in the field for each individual procedure and approach and can easily be referenced.<sup>30</sup>

Next, when performing laparoscopic surgery, there is a loss of tactile feedback used by surgeons to differentiate tissue types. Using two laparoscopic instruments and frequently touching objects in the visual field provides some sensory input. Again, this maneuver also assists the surgeon in maintaining a three-dimensional orientation to the two-dimensional video image.

### **Educating surgeons in laparoscopic techniques**

Concerns about the adequacy of surgical education have been increasing. Countless problems exist in surgical education, such as increasing constraints imposed on operative time, the changing patient population at teaching hospitals, heightened medicolegal considerations, and the higher cost of running residency programs. With laparoscopy, these problems are amplified and apply not only to surgical residents but also to all surgeons in practice who want to keep up with new techniques. Thus, there is an urgent need to improve on the current quality of residency and post-residency training methods.

In order to progress, educators in urology need to examine the teaching methods being used today critically and to have knowledge about the background literature, as general surgery has been investigating methods to educate surgeons in laparoscopic technique since laparoscopic cholecystectomy appeared on the scene in the mid-late 1980s.<sup>31,32</sup> With the initial high rate of complications with this procedure and even some reported deaths, they have had to re-evaluate how to educate and train surgeons to perform such procedures.<sup>33-35</sup> This literature contains a wealth of information that we can use. Mistakes can be avoided if we are willing to take the time to educate ourselves and apply the information. Dogma needs to be put to rest and we need to base our teaching on scientifically based facts.

### **Laparoscopic skill development is related to recent and ongoing laparoscopic training and experience**

Open surgical skills are based on an ensemble of techniques that can be transferred from one procedure to another. During open surgery training it has been demonstrated that learning basic surgical skills allows surgical residents to build on those skills for more

complex or related skills. Transfer of training (TOT) is the term used for this process and it is a necessary process in the development of open surgical technical skills.

Many assumed that TOT from open skills takes place to laparoscopic skills and for years we have heard the comment that 'the best laparoscopic surgeons are the best open surgeons,' but studies by Figert et al refute this.<sup>36</sup> In their study, transference of open surgical skills to laparoscopic skills was specifically examined and it was assumed that more experienced open surgeons have shorter learning curves for new surgical procedures secondary to TOT. No evidence was found for TOT from open surgical experience to newly introduced laparoscopic knot-tying techniques or from one skill training session to a different skill session at least 4 hours later. More notable is that their data suggests that specific laparoscopic skills might not be transferable to acquisition of different laparoscopic surgical skills. These findings may explain why surgical residents and experienced open surgeons do not differ significantly when learning new laparoscopic skills. These findings further support what has been recognized by others but never documented: laparoscopic skill development is related to recent and ongoing laparoscopic training and experience. Collectively, this information supports the concept that specific minimally invasive surgery training is needed to develop laparoscopic surgery skills.<sup>36</sup>

### **Inherent surgeon characteristics**

It has been a commonly held assumption that younger surgeons have a natural advantage in the development of surgical skills. The affects of age, gender, lateral dominance, and prediction of open operative skills among general surgery residents was examined. In one study investigators found that, while age influenced pure motor skills, neither age nor pure motor skills are necessarily important for open operative skills. In fact it was stated that 'contrary to surgical folklore, pure psychomotor skill (manual dexterity) is not the major dimension distinguishing the proficient surgical performance from the mediocre.' It was found that the components necessary for superior open surgical skills included nonverbal, visuospatial problem-solving abilities (i.e. the capacity to rapidly analyze and organize perceptions based on multisensory information) and the ability to distinguish essential from nonessential detail even when the 'signal-to-noise ratio' is high.<sup>18,19</sup>

Rosser et al in the development of the 'Yale Laparoscopic Boot Camp' also found that age and sex did not play a dominant role in skills outcome.<sup>37</sup> All participants who attended the courses, regardless of age, sex, and previous training, learned intracorporeal suturing and performed an anastomosis. The performance of all participants improved in the study. Collectively, the residents took marginally longer to complete an anastomosis, although their suturing time was not significantly different from that of a trained surgeon. The difference between the residents and trained surgeons was felt to be due to a lack of experience in performing anastomosis rather than in suturing skills. Residents took more time to perform the cup drop drill, which requires considerable depth perception to the two-dimensional environment. However, residents performed significantly better than trained surgeons in the triangle transfer drill, which requires two-hand skills as well as depth and spatial orientation. No difference was noted in the performance of male and female residents in performing either drills or suturing exercises. The finding that trained

females took a longer time to complete suturing exercises and rope pass drills was only marginally significant ( $p < 0.5$ ). Rosser et al concluded that age and experience might influence some types of dexterity drills, but overall they do not seem to play a dominant role.<sup>37</sup>

In a related study, Hayward et al compared the abilities of male and female residents in six areas: ethics, judgment, technical skills, knowledge, interpersonal skills, and work habits. Again, no difference was found between female and male residents.<sup>38</sup> Schueneman et al found that left-handed residents were more reactive to stress, more cautious, and more proficient on a neuropsychologic test of tactile-spatial abilities than right-handed counterparts. Although these traits correlated positively with rated open operative skills within the left-handed group, the group received consistently lower ratings than did right-handed residents. They hypothesized that the 'inconvenience' of assisting left-handed residents may overshadow attending surgeon's perceptions of their innate abilities.<sup>19</sup> More recently, Hanna et al re-examined psychomotor skills for endoscopic manipulations for minimally invasive surgery and the differing abilities between right- and left-handed individuals.<sup>39</sup> They found that right-handed subjects performed better with either hand in terms of error rate and first-time accuracy than left-handed individuals. Their findings are consistent with previous reports on psychomotor studies that showed left-handed people have poorer spatial perception than right-handed subjects.<sup>40–43</sup> However, many others have not supported this difference.<sup>44–46</sup> Right-handed subjects also performed tasks in a shorter execution time but with more force on the target than left-handed individuals. The longer execution time by the left-handed subjects with application of less force on the target are in agreement with the reported observations of Schueneman et al and appear to support the concept that left-handed surgical residents are more cautious than right-handed counterparts. These particular findings demonstrate significant, neuropsychologically based differences among surgery residents that pose unique challenges to persons responsible for their education and training.

### **Teaching surgical skills outside the operating room—the influence of technology, inanimate models, and simulators**

Teaching skills in the operating room is inefficient, and expensive, and learning on patients is no longer acceptable. Current curriculums have been designed to train residents outside of the operating room, but no consensus exists as to what type of training is appropriate and how much training is necessary to effectively impact operative performance.<sup>13,47</sup> Rapid acceptance of laparoscopic surgery has resulted in high complications, especially with novice surgeons. It has been consistently reported that surgical complications occur most frequently during the first 10 procedures that the laparoscopic trainee performs.<sup>32,33,35</sup> The importance of adequate education and accrue ment of appropriate skills before attempting procedures on live patients have been highlighted by this high rate of serious complications.<sup>48</sup>

While it has been proven that texts, lectures, and video are important tools for developing insight into the essentials of an operation, they are of limited value due to their didactic nature. Naturally, laboratories with simple inanimate models or live animals

for hands-on training allows each surgeon to practice prior to performing the procedure on a patient and therefore they have been included in the current surgical training models. Inanimate models rather than animal models are popular for training outside the operating room because they are reproducible, offer unlimited practice, are readily available and require no supervision.

In 1997 Martin et al examined the reliability of assessing the technical skills of surgical trainees using live vs bench formats. The bench model simulation gave equivalent results to use of live animals with their testing format.<sup>49</sup> Further studies were conducted and it has been proven that practice in these simulators results in an improvement in the skills practiced and assayed in the same simulator.<sup>50</sup>

These simulators allow for practice at various skill levels and, in addition, since many surgeons may not have access to an animal laboratory facility, it is reasonable to use such inanimate models; however, there are drawbacks. The initial simple box laparoscopic trainer was not designed to simulate a specific surgical procedure and its only function is to serve as a fundamental training device for basic skills used in the majority of surgical operations. Also, the more simple and basic training boxes do not mimic human anatomy and living tissue. Furthermore, Jordon et al argues that the use of a box trainer fails to provide trainees with any clear indications of their level of manual with their peers.<sup>51</sup> dexterity, their progress in training, or even a comparison

Recently, Scott et al showed that skills acquired from dry labs using the Guided Endoscopic Module (GEM, Karl Storz Endoscopy, Culver City, California), a training system, were transferable to the operating room.<sup>52</sup> Until this time, studies in the outcome of dry lab training measured improved skills on the same simulator on which the training took place and not in the operating room, so the true transfer of skills training was unknown.

Once the use of basic simulators was shown to be effective in skill acquisition, the need to make them more sophisticated or lifelike came into play. Use of multimedia interactive computer-based training used in such areas as the military, high-tech industries, and even the business world, was examined. Given the fact that multimedia interactive computer-based training has been shown to decrease the learning curve by 60% and increase retention by 50% when compared to traditional didactic training, its use in laparoscopic surgical training was attractive.<sup>53</sup> Multimedia interactive programs have the advantage that they are self-directed, self-paced, and interactive, which is consistent with the proven methods of adult learning. Since programs can be developed from the experience of many surgeons, the emphasis is placed on correct surgical principles for the performance of a specific procedure. The steps of the procedure and the variety of presentations of complications possible at each step of the procedure become the focus, and the experience of many becomes additive to the teaching process. Multimedia interactivity, input from many experts, and an ability to individualize the pace of the learning experience are unique advantages to these training programs.<sup>22</sup>

Using such a program, the Minimally Invasive Surgical Trainer Virtual Reality system (MIST VR, Mentice, AB, Gothenberg, Sweden), Seymour et al in a randomized, double-blinded study found improvement in the operating room performance of residents.<sup>54</sup> This appears to be the first study demonstrating that it is feasible to train operative skills using virtual reality in surgical trainees without extensive prior minimally invasive experience that transfer to the real environment, i.e. the operating room. Further analysis of virtual

reality training for technical error reduction, surgical judgment, or even as a means of certifying surgeons remains to be addressed.

Finally, European physicians have not had the luxury of using animal models for surgical training, and practicing in the patient setting has been frowned upon. Consequently, other methods of surgical education and training have been sought sooner and the European community has undergone a multi-institutional project, named the Minimally Invasive Surgery SIMulator (MISSIMU), with the joint efforts of clinical European centers and two European Industries.<sup>55</sup> While other projects have utilized three-dimensional reproduction to represent human anatomy, this project is more advanced in that its goal is to provide a virtually 'living' human body, inside which it would be possible to perform laparoscopic surgery with tactile sensations and force feedback.<sup>56,57</sup> We await the outcomes of this project.

### **What training equipment is necessary?**

Training can be obtained with even the most meager budget. Keyser and colleagues compared a simplified mirrored-box simulator (Simuview) to the videolaparoscopic cart system.<sup>58</sup> They found that laparoscopic skills can be measured objectively in a videolaparoscopic cart simulator system and the scores were sufficiently sensitive to distinguish differences in performance between residents at different levels of training. The low-cost mirrored-box simulator also gave a reasonable reflection of relative performance of laparoscopic skills. Therefore, if these skills demonstrate transfer to the operating room, a practical, effective basic laparoscopic skills training and evaluation can be accomplished without the need for costly equipment.

Gallagher et al subjected the MIST VR to a prospective, comparative evaluation with traditional laboratory training methods for psychomotor skill (manual dexterity) acquisition only.<sup>59</sup> They found that participants trained on the MIST VR performed significantly better than casematched participants trained on a traditional box trainer and a control group who received no training. Although manual dexterity is important for surgical procedures, as recalled from the previous sections, it is only a portion of the skills needed for laparoscopic procedures and, again, the cost vs benefits need to be carefully weighed in this situation. Although the incorporation of new training tools such as multimedia interactive programs into surgical training is exciting, there are still many issues to be resolved. Although presumed, will the increased knowledge and comfort levels afforded its user translate into shortened learning curves and fewer complications? Although this benefit has been shown in other industries, does it also apply to laparoscopic surgery?

Many simulators are appearing on the market but, to date, no comparison studies have been performed. The key question—Is there transfer of training?—has not been addressed for all simulators. Remembering the sage advice that 'a fool and his money are soon parted', one has to examine these simulators critically and look at scientific data, the actual skill transfer to the operating room, and not at advertisements or endorsements from 'laparoscopic superstars'.

### **Experienced surgeon—another key component for laparoscopic teaching**

Once you have embarked on a training model, what else can you do to optimize laparoscopic teaching? The Laparoscopic Education Study Group identified a teacher base skilled in laparoscopy as a key component to establishing a successful education program. Without this, a training program limits preceptorship and tutorial portions of resident laparoscopic education.<sup>60</sup>

To enhance resident training, programs have hired an experienced laparoscopic surgeon. Fowler and Hogle looked at the impact that this had on their program and found that with the addition of an experienced laparoscopic surgeon in a resident training program laparoscopic cases in which residents participate increased by more than 100%.<sup>61</sup> Laparoscopic training sessions and minimally invasive research projects also increased measurably.

More and more residents desire to learn the techniques and acquire the skills needed to perform advanced procedures. Although several fellowships in laparoscopic urology are available, demand for these positions far exceeds their availability and there is no uniformity in the education of these fellows. Numerous residency programs have hired such trained laparoscopic surgeons, often by appointing that surgeon to a position such as 'director of minimally invasive surgery'. The acute goal has been to expose both faculty and residents to more advanced laparoscopic procedures, with the ultimate goal of teaching them to perform the procedures. Our personal communications with other fellowship-trained laparoscopic surgeons acting in this role revealed that this endeavor has received results ranging from enthusiasm, to trepidation, and even animosity in various institutions.

### **Costs**

A final concern is the cost involved with training laparoscopic skills. In 2000, the list price for a video trainer (guided Endoscopic Module) ranged from \$215,000-\$285,000 depending on the quality of video-imaging equipment installed. At the University of Texas Southwestern Medical Center, a total of 186 residents train in general surgery, urology, and gynecology. The cost of training residents using the video trainer was estimated as \$270 per graduating resident.<sup>52</sup> In comparison, Bridges and Diamond,<sup>62</sup> at the University of Tennessee Medical Center-Knoxville, estimated that using operating room time to train residents costs about \$48,000 per graduating resident.

Intuitively, training outside of the operating room seems cost-effective, but a comparison with an institution that hires a laparoscopic-trained staff to teach and perform complex laparoscopic cases with simpler methods needs to be made. Staff can generate revenue while the simulator cannot.

### **How does one measure operative skills?**

The teaching model is in effect: now one must answer how does one measure success or progress? A major pitfall of training models is the lack of objective assessment used to document improvement or proficiency. Many studies use time to complete a task as the sole assessment of competency. Time assessment alone does not document the steps taking place between the starting and stopping of the stopwatch. It is believed that using time alone to measure skill level overestimates the true levels of laparoscopic skill. In fact, investigators using a laparoscopic skills assessment device that precisely measures movements of instruments during performance of laparoscopic manipulative skills found that the learning curve for operator speed is shorter than the learning curve for operator accuracy.<sup>63</sup> Therefore, laparoscopic accuracy is a more sensitive indicator of skill acquisition than measurement of laparoscopic speed, suggesting a minimum of both variables needs to be considered in developing teaching modules and proficiency standards. Common sense suggests that the main aspects of evaluation should concentrate on how the task is completed rather than on how fast the task is completed.

### **Operating room skill assessment**

Global assessments of operative performance based on direct observation have been extensively studied in the context of open operations and simulations. Reznick and colleagues have shown that global assessments are superior to checklists in validity and reliability.<sup>23</sup> Global assessments are not procedure-specific but rate skill using general performance criteria. Therefore, such assessments may be used for different operations without modification and appear to be the best tool currently available for evaluating skill level in the operating room. Unfortunately, global assessments are almost as time consuming as the earlier checklists and a dedicated evaluator must be present for enough of the operation to draw conclusions about skill level.<sup>64</sup> Shortcuts using video monitoring have been attempted. Even if the assessment is applied to videotaped footage, so that the evaluator need not be present during the case, the entire operation must be viewed. Further attempts to maximize the efficient use of the reviewer's time looked at the use of edited videotaping. Skill assessments were made from the edited tapes and compared to direct observation assessments.<sup>26</sup> It was discovered that the videotape evaluations did not demonstrate the difference in skill level between the trained and control groups that the direct observation assessments had detected. Also, correlation between videotape and direct observation scores were poor, and interpreter reliability suffered as a result of the videotape format.

The edited videotape contained only visual information and no audio or visual information from the external operating room environment was recorded. It was believed that this information was crucial to the assessment process. For example, were erratic movements attributable to a lack of resident dexterity or to interruption by the faculty for the purpose of teaching? Equipment problems were not detectable from the videotape and could be misinterpreted as unnecessary delays related to resident skill. Residents were



asked to vocalize their operative plan and to identify anatomic landmarks during the evaluation and without sound the videotaping of the operation did not capture this information. Other areas that the evaluators could not assess included 'knowledge of instruments', 'use of assistants', and 'knowledge of specific procedure'. Again, this missing data on the videotape were believed to be the reason that videotape assessments did not correlate with assessments performed in the operating room.<sup>26</sup> The investigators concluded that the wealth of information in the operating room was important to the evaluation process, including audio or visual information from the external operating room environment.

### **Role of robotics in education**

Robotics represents the current frontier in minimally invasive procedures. Surgeons have recently been sorting through the facts and myriad of misinformation, trying to qualitatively and quantitatively analyze their effects. Sung and Gill compared the da Vinci (Intuitive Surgical, Inc., Mountain View, California) and ZEUS (Computer Motion, Inc., Goleta, California) systems and found that the learning curve and operative times were shorter, yet this may be biased by their being proficient at extremely difficult laparoscopic procedures without the use of robotics.<sup>65</sup> Dr Menon looked at open prostatectomies vs laparoscopic vs robotic prostatectomies.<sup>66</sup> His data are confusing due to the fact that different surgeons were involved at different arms. Experienced laparoscopic surgeons performed the laparoscopic procedures, while Dr Menon—using himself as the only inexperienced laparoscopic surgeon—performed robotic prostatectomies; however, he had previously assisted in over 100 pure laparoscopic procedures and the term 'inexperienced' may be inaccurate. Lee and colleagues have stated that in their experience there is a difference in the learning curve with using robotics but their study uses time for an objective parameter, which when used alone is insufficient. As discussed earlier, performing a procedure quicker does not correlate with better results and, more importantly, failing to consider objective assessments of accuracy may lead to overestimating laparoscopic proficiency.<sup>67</sup>

Turning to our general surgery colleagues, Prasad et al<sup>68</sup> reported that laparoscopic tasks performed with ZEUS robotic assistance allowed for increasing speed and consistency while maintaining precision over multiple repetitions, whereas Dakin and Gagner<sup>69</sup> recently reported that basic laparoscopic task performance was generally faster and as precise using standard instruments when compared to the ZEUS robotic surgical system and the da Vinci Surgical System. In their trial when performing fine tasks neither robotic system was faster than standard instruments. Precision with the robots was enhanced over the standard instruments and in this respect may offer an advantage.

Here, as in other instances, TOT needs to be evaluated; also, inexperienced laparoscopic surgeons are the area of concern and testing in these subjects is paramount. Recent concerns about the availability of the robot and canceling cases because the surgeon does not have the skills necessary to complete the case purely laparoscopically were raised at the World Congress of Endourology 2002. Will complication levels be greater if surgeons who lack the skills to perform conventional lap skills short cut training and use the robot? Which is the correct order to proceed when training for laparoscopic

procedures: pure laparoscopic rather than robotic, or vice versa? A better understanding of how robotics affects the learning curves will allow for modifications in the training experience with this new technology. Again, efforts need to be made to examine the appropriate teaching of laparoscopic skills closely to avoid major complications and maximize efficiency in training.

### **Telepresence surgery**

The basic concept of telepresence surgery is that an experienced laparoscopic surgeon at a central site can offer assistance, mentored intervention, or guidance to colleagues less experienced at distant sites or even in nearby operating rooms. This concept became a reality in 1996 when Moore and Kavoussi published one of the first experiences in telepresence surgery.<sup>4</sup> However, although telemedicine mentoring and assistance during the learning curve have been successfully implemented in studies and would provide an acceptable bridge for those at the beginning of the laparoscopic learning curve, the medicolegal issues, costs, and scheduling constraints continue to hinder its advancement in the United States. Other uses of telepresence surgery have been in teaching medical students.<sup>70</sup> Uses for telepresence surgery will continue to grow and its full potential use is still being determined. Chapter 55 gives a more comprehensive overview of surgical robotics and telepresence surgery.

### **Courses**

Adaptation rates or skills transfer for trained surgeons attending the standard equipment company-sponsored courses remain disappointing. Follow-up surveys on surgeons who participate in these standard courses has revealed a low likelihood of adopting the 'taught' procedure.<sup>2,3,5</sup> These surveys have also shown that if the participants do not seek further training or do not have experienced surgeons to assist or proctor them during their initial cases, complication rates are increased. Furthermore, in advanced laparoscopic procedures, even when the inexperienced surgeon knows the complications that occur during the learning curve phase, the complication is not avoided by this knowledge. Quicker identification may be made from the knowledge but, again, prevention of complications is not reduced. On the horizon is the use of internet-based 'courses' to educate surgeons. Webcast courses make any location where a computer is installed a classroom and programs without expert faculty can be exposed to minimally invasive techniques via this media. The course may be interactive or a simulation to enhance one's skills. Investigators are moving in this direction and the educational results remain to be seen.<sup>71-73</sup>

Suggestions on what to look for in a laparoscopic training course include:

- What are the course objectives and can they be met in the suggested format?
- What are the basic skill requirements and how may one obtain these skills if they are needed prior to the course?
- Are the principles of adult education being followed?

- What reinforcement material will be included to enable one to practice the skills or review the technique needed to successfully complete the skill being taught at the course?

The course should be used to hone your skills, correct your bad habits, review laparoscopic anatomy, review how the 'experts' handle the problems encountered in the laparoscopic approach, and review the complications and how to remedy or recognize them. Reinforcement material such as an interactive CD-ROM should allow one to 'practice' the procedure at home to ready oneself for performing the procedure independently or a videotape reviewing technique, problems encountered, and troubleshooting for such problems commonly encountered during the procedure also seems appropriate. Edited tapes of the surgical procedure, although highlighting the 'laparoscopic superstar's' talent, really appear to add little to the novice's learning experience, as the editing leaves out any problems that arose during the case and how to deal with them. Another important point to be aware of is that skill transfer from the course to the operative suite is higher when attending the course with a colleague or another person involved with the operating team.<sup>2</sup>

### **Moore simplified model of laparoscopic training**

Currently, laparoscopic intracorporeal suturing is the most difficult exercise to master in the minimally invasive environment. Yet several investigators have shown that with training even the most inexperienced individual can learn to suture. Champion et al taught surgically inexperienced medical students to complete an extracorporeal suture with a 3-throw knot in an average of 3 min 12 s, while Moore et al taught surgically inexperienced first-year medical student intracorporeal laparoscopic suturing in which they had to complete two separate knots.<sup>8,12,74</sup> In this study objective criteria included time to complete the task and knot quality—Was the knot squared? Did it slip?—and each knot's breaking strength was recorded in newtons. The average time to throw two 2–0 silk knots was 7.1 min and 5.2 min for 4–0 silk. These outcomes are excellent when one compares the results of Pattaras et al, who reported that experienced laparoscopic surgeons using 2–0 polyester suture tied knots with 5 half hitches in an averaged 5.08 min/knot.<sup>75</sup>

The fact that training is needed for laparoscopic surgery is not disputed, but today there exists no consensus on which tasks are suitable, how much training is needed, and who should be trained. Below is an example of our training model. Based on adult educational principles, it provides instant feedback to trainees, which we believe accelerates the laparoscopic learning process, and one-on-one interaction, which we believe avoids the pitfalls of trainees developing bad habits that need to be 'unlearned' if the learning was done entirely on a self-directed individual basis.<sup>76</sup>

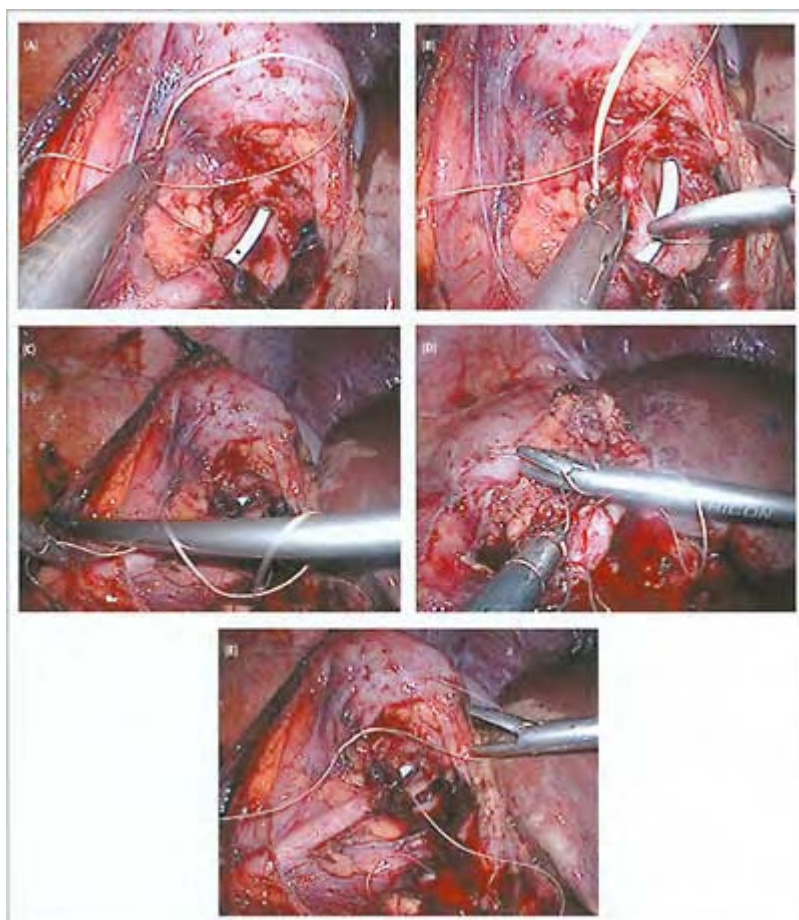
In our program we start with didactic lectures with actual dry lab reinforcement to meet cognitive and technical goals. Subject material covered includes but is not limited to:

1. Light sources, video cameras, insufflators.
2. Pneumoperitoneum: physiologic changes and entry to and exit from peritoneal cavity.

3. Energy sources in laparoscopy.
4. Laparoscopic anatomy.
5. Laparoscopic procedures.

### **Developing basic skills**

Drills to increase ambidexterity seem obvious. In our model, subjects are asked to use their non-dominant hand during everyday activities—brushing their teeth, eating, dressing, answering the phone, etc. Next, to overcome what we term ‘right/left hand/brain dominance’, a series of tracings or patterns are placed on a table in front of a mirror. While looking only into the mirror the pattern is traced right to left and left to right using both the dominant hand and non-dominant hand. The tracings start out very simple and become more and more complex. Instrument use has been previously described and is again demonstrated. Each individual takes time to acclimate to the instruments in a simple video box. The bounce technique (moving the instruments across the field in a stepwise fashion to get to the intended spot) to find one’s instruments is taught and the subject practices this until moving the instrument directly to the intended position is not a problem. Subjects are taught to place their trocars in a diamond pattern and reminded that they are to have both hands on an instrument at all times. According to Hanna et al, a combination of a 60° manipulation angle with 60° elevation angle provides the shortest execution time and highest performance score when evaluating optimal port locations for intracorporeal knot tying and this is demonstrated.<sup>77</sup> Appropriate laparoscopic instruments are used to transfer various objects, including but not limited to rope, Penrose drains of various size, washers, needle caps, navy beans, etc. Next, to further laparoscopic spatial orientation, items are placed within other objects or onto a peg of varying sizes using both dominant and non-dominant hands. This is followed by two-handed drills: using two graspers and removing an object from a dish while placing another object into a second dish simultaneously; holding the camera with one hand and moving a washer onto a peg with the other hand; holding an 18-gauge needle in the air with one instrument, uncapping it and placing it down on the surface, picking the pieces up and in midair recapping the needle. Principles of retraction and countertraction are reviewed and demonstrated for cutting objects or various shapes from gauze sponges. A pattern is drawn on a gauze sponge and suspended in the training box at various positions from the ‘bull’s-eye’ position in the working zone and later the pattern is moved to the right or far left of the working area. Next, subjects are asked to try various needle drivers for ease and comfort. A gate made of cloth tape placed between two posts is placed in the training box. Using a needle driver in each hand, a needle is passed from right to left and back again through the gate from left to



**Figure 11.1** Basic steps of intracorporeal knot tying: (A) Using a needle driver the needle is grasped in the middle or proximal third of the shaft of the needle. (B) A second needle driver is used for countertraction on the tissue and the needle is passed from left to right and right to left or vice versa. (C) Typically, we initially employ a surgeon's knot to lock the suture in place. When possible, the memory of the suture is used to our advantage to

form the loops around our needle driver. (D) The end of the suture is grasped and drawn through the loops previously thrown around the driver. That the knot is squared is checked and the knot tightened. (E) The above steps are repeated as needed for the number of throws wanted for each specific suture.

right. Appropriate needle angle is discussed and needles of varying sizes are used. At least four positions are used for the gate, with the starting position being the bull's-eye zone with the gate straight up and down. As the subject masters this, the gate is spun to say a right oblique position and the exercise repeated (Figure 11.1).

### **Complex skills**

Once the subject is comfortable with these maneuvers, a demonstration of suturing techniques is reviewed. Several papers exist on laparoscopic suturing.<sup>74,78-80</sup> Correct suture length for tying is discussed, and tricks to aid one in righting the needle, dealing with too short a suture, too long a suture, or what to do if the needle or suture breaks are reviewed and demonstrated. Hints such as gripping the needle in the middle or at the proximal end, holding the needle  $>90^\circ$  to the instrument axis, and inserting the needle between  $80^\circ$  and  $100^\circ$  angle are reinforced, as this aids in improving task accuracy.<sup>81</sup> Under direct supervision, the subjects are allowed to master the conventional suturing and knot. Instant feedback is given to facilitate learning and decrease errors. Notable time-wasting maneuvers are pointed out or obvious need to continue to work on deficits is noted. Drills or further homework are given to compensate for the observed weaknesses by the fellowship-trained surgeon. As evidenced by Emam et al, the subjects are taught that optimal suturing with better quality and reduced execution time is accomplished with vertical suturing toward the surgeon with isoplanar monitor display of the operative field. It was demonstrated in their study that poorer performance was seen with horizontal suturing and was accompanied by more muscle work and fatigue. Also, they found that horizontal suturing did not improve by monitor display of the incision in the vertical plane.<sup>82</sup> Although one cannot always set up the operative field to accommodate vertical suturing, the subjects are made aware of the fact, so that when feasible they can 'help themselves' more easily perform the task which aids in keeping operating room time to a minimum. Once suturing and knot tying is mastered, the subjects are asked to sew together the finger of a latex glove with an ~1–2 inch rent. We have found that the glove is inexpensive and if not handled with care the suture easily rips the latex, reinforcing appropriate tissue handling. Once mastered, more difficult exercises are given such as sewing the finger back on the glove and suturing Penrose tubing of various sizes together at various positions and varying sizes. Maneuvers for

hemostasis are reviewed and hypothetical situations are given with a walk through of how one may handle the problem laparoscopically. We believe that rehearsal of such situations decreases anxiety and errors when they appear in the actual operating room. Subjects become familiar with instruments such as clip applicators, and instructions with stapling devices are also included. Finally, a procedure such as a pyeloplasty followed by a nephrectomy in the animal laboratory is scheduled. Subjects are brought into the animal laboratory and the subject performs the procedure with anatomy review, surgical principle review, and further instruction as it arises. Here, as always prior to starting the procedure, a plan is discussed how the laparoscopic procedure will be safely converted to a hand assist or even an open procedure, what role each individual will play in opening, and who will decide to open; also, appropriate open instruments will be discussed and checked for presence in the operating room. Discussion on how to surgically assist is also given. Here is a chance to also discuss and demonstrate reverse alignment conditions and the maneuvers to improve performance. At times the surgeon has to operate ahead of the camera and, as a result, the image displayed on the monitor will be an inverted mirror image of the operative field, so that the view is upside down and reversed left to right (reverse alignment). While most surgeons will simply transfer the scope to another port, this may result in less optimal angles to work from and adds time to the operative case. Basically, we have found, like Cresswell et al, that the effect on performance produced by reverse alignment of the scope and instruments can be overcome by simply turning the camera through 180° or, if available, digital electronic processing will aid in reducing execution time and execution-time errors.<sup>83</sup> Again, the subjects are given these aids so they may continue operating under optimal conditions in a timely fashion.

Lastly, we believe that videotaping the procedure is a valuable learning tool. Subjects are encouraged to review their performance and look for further areas of improvement, look for wasted movement, review laparoscopic anatomy, review the steps in the procedure while reviewing possible complications at each step and what methods can be performed laparoscopically to remedy the situation. They are asked to make a game plan on how they could improve the overall performance of the procedure.

## Conclusion

It has been demonstrated that minimally invasive surgery is safe but only in experienced hands. Being a competent surgeon is more than having psychomotor skills; rather, nonverbal, visuospatial problem-solving abilities and the ability to distinguish essential from nonessential detail even when the signal-to-noise ratio is high appear crucial to superior technique.

Recently, it has been determined that the skills necessary for laparoscopic procedures are unique, and open operative skills often do not transfer. Educational models for open procedures are lacking and not valid for laparoscopic procedures. A critical review of our educational process with the aid of general surgery's own experience in laparoscopic education needs to be done. The need for out-of-the-operating room training is evident, but there is no consensus on which skills need to be taught and how much training is suitable. Realistically, developing an all-inclusive laparoscopic training course may never be done, but we can strive to make our education system better by requiring rigorous

scientific validation of the educational interventions used. Application of adult educational principles for adult learning is a must to facilitate learning. Training has to be objectively monitored using proven methods, with documentation of TOT from the educational model to the operating room.

Laparoscopic surgery was once thought of as the future and today, despite several advances with virtually all open procedures being replicated laparoscopically, the final chapter still remains to be written. As always, we must continue to adapt so that we can continue to grow.

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## **Part II**

# Adult minimally invasive urologic surgery

## 12

# Laparoscopy in renal transplantation

Tanmay Lal and Lloyd E Ratner

### Introduction

Over the last decade laparoscopy has become an increasingly important tool in the technical armamentarium of the transplant surgeon and those other surgeons that operate on renal transplant patients. Although the recipient operation for renal transplantation has not yet been performed laparoscopically clinically, technical advances in laparoscopic instrumentation and surgical robotics make this now theoretically feasible. It is just a matter of time before this is accomplished. However, the application of minimally invasive techniques has revolutionized some aspects of the management of renal transplant recipients and live kidney donors. Laparoscopic live donor nephrectomy and laparoscopic marsupialization with internal drainage of perirenal allograft lymphoceles are now performed routinely. Also, the performance of a variety of other laparoscopic procedures has been reported in renal transplant recipients.

This chapter discusses the utility and pitfalls of laparoscopic surgery in the renal transplant recipient and the live kidney donor. In both these patients one overriding concern is the maintenance of optimal renal function in the solitary functioning kidney. Thus, the physiologic affects of pneumoperitoneum must be appreciated and proper intraoperative anesthetic and fluid management applied.

### Physiology of pneumoperitoneum and its relationship to the kidney

#### *Physiology of Pneumoperitoneum*

Carbon dioxide pneumoperitoneum causes a variety of physiologic responses during laparoscopy. The physiologic changes observed during pneumoperitoneum are due to alterations in hemodynamics, pulmonary function, acid-base balance, and changes in hormonal secretion. Insufflation pressures used during most laparoscopic procedures range between 12 and 20 mmHg. The inferior vena caval and portal venous pressures are observed to increase with a concomitant decrease in flow in the superior mesenteric artery and portal vein.<sup>1</sup> There is also a decrease in venous return to the heart. Central venous pressure is either unaffected or only minimally elevated.<sup>2</sup> Cardiac output and stroke volume are decreased or remain unchanged. CO<sub>2</sub> pneumoperitoneum causes hypercapnia and acidemia that can initiate pulmonary hypertension and systemic vasoconstriction.<sup>3</sup>

There is a linear increase in peak airway pressure due to the positive pressure ventilation.<sup>4</sup> This is due to the upward displacement and distention of the diaphragm, causing a decrease in thoracic cavity space. With CO<sub>2</sub> pneumoperitoneum, persistent respiratory acidosis is a complication due to the need for increased minute ventilation. In individuals at risk for the development of hypercapnia, it is advantageous to monitor the patient's acid-base status intraoperatively with continuous end-tidal carbon dioxide monitoring as well as arterial blood gas monitoring.<sup>5</sup> Antidiuretic hormone levels are shown to increase upon insufflation. Other hormones and metabolites are increased during the stress of the operation—glucose, cortisol, prolactin,  $\beta$ -endorphin, epinephrine, norepinephrine, dopamine, and interleukin-6 (IL-6).<sup>6</sup>

### *Renal responses to pneumoperitoneum*

The net affect of these physiologic perturbations on the kidney is a decreased renal blood flow and decreased urine output. However, London and colleagues<sup>7</sup> have elegantly shown in a large animal model that these affects can be abrogated with volume loading. This can be accomplished with either isotonic or hypertonic solutions. Therefore, in many cases, particularly during laparoscopic live donor nephrectomy, larger volumes of intravenous fluids may need to be administered intraoperatively to promote a brisk diuresis subsequently in the renal allograft. Although transient changes in renal function can be observed during pneumoperitoneum that can result in either allograft dysfunction or acute tubular necrosis, no long-term affects of pneumoperitoneum have been described.<sup>8,9</sup> Additionally, in a rat model, Lee et al<sup>10</sup> have demonstrated that prolonged pneumoperitoneum (5 hours) failed to cause any lasting histologic changes in the kidney. However, studies that have examined the impact of CO<sub>2</sub> pneumoperitoneum on renal function have all studied kidneys in the native position. It is unknown whether denervating a kidney and the extra-anatomic position of renal allografts in the lower abdomen would cause the responses to pneumoperitoneum to be altered.

A number of centers have advocated a gasless approach to laparoscopic live donor nephrectomy, mainly to eliminate the physiologic changes experienced by the kidney during pneumoperitoneum. The physiologic responses to a gasless approach employing abdominal lifters have not been well studied.

## **Laparoscopic surgery in live kidney donors: laparoscopic live donor nephrectomy**

### *History and rationale*

Open live donor nephrectomy via a flank approach was first performed in 1954 for the famous identical twin transplants. For 40 years the operation went virtually unchanged. In 1994 Gill et al<sup>11</sup> described the first experimental series of laparoscopic live donor nephrectomies in a large animal model and demonstrated that adequate lengths of renal vessels and ureter could be obtained and that the kidney could function appropriately once transplanted. In 1995 Kavoussi and Ratner<sup>12</sup> performed the first clinical laparoscopic live donor nephrectomy with the goal of decreasing the economic and

logistical disincentives to live kidney donation. Although highly controversial at first, laparoscopic live donor nephrectomy has been broadly adopted by transplant centers worldwide and is rapidly becoming the standard of care.

### *Donor results*

A variety of investigators<sup>13-16</sup> have now shown that relative to the open live donor operation performed through a flank incision (either with or without rib resection), laparoscopic live donor nephrectomy results in decreased parenteral analgesic requirements, decreased analgesic requirements post-discharge, earlier resumption of oral intake, shorter hospitalization, quicker recuperation, earlier return to full activities, and an earlier return to employment (Table 12.1). Also, in a prospective randomized series of hand-assisted laparoscopic live donor nephrectomies vs open donor nephrectomy via a flank incision without rib resection, Wolf and colleagues at the University of Michigan<sup>17</sup> have reported that the donors undergoing the laparoscopic operation feel '100% normal' at a median of 33 days, whereas, less than 50% of the open donors feel '100% normal' 4 months postoperatively ( $p=0.032$ ).

The donor complication rate of laparoscopic live donor nephrectomy is roughly equivalent to that of the open donor operation. However, the spectrum of complications is somewhat altered. We conducted a survey of 130 institutions that performed  $\geq 3456$  laparoscopic live donor nephrectomies. This survey revealed that the most common complication was need for transfusion (1.6%), followed by wound infection (1.4%), bowel obstruction (0.4%), incisional hernia (0.3%), vascular injury (0.3%), deep vein thrombosis (0.2%), diaphragmatic injury (0.2%), splenic injury (0.1%), pulmonary embolus (0.09%), bowel injury (0.09%), and sepsis (0.03%). There were no mortalities reported for the series, indicating that the mortality of laparoscopic live donor nephrectomy is likely to be on the same order of magnitude as that of 3 per 10,000 for the open live donor operation.<sup>18</sup>

### *Recipient results*

Importantly, laparoscopic live donor nephrectomy has not deleteriously affected the recipient. Early renal function, incidence of delayed graft function, incidence of rejection, severity of rejection, incidence of ureteral complications, incidence of vascular thrombosis and long-term renal function are comparable between recipients of laparoscopic procured live donor kidneys and those obtained from donors undergoing the open operation<sup>19,20</sup> (Figure 12.1).

### *Preoperative donor work-up*

The evaluation of the potential laparoscopic donor is similar to the evaluation for the open donor (Figure 12.2). Guidelines have been published by the American Society for Transplantation<sup>21</sup> for the evaluation of all potential live kidney donors. Multiple previous upper abdominal surgeries may serve as the only contraindication to the laparoscopic approach. Obesity is not a contraindication



**Table 12.1** *Results for open live donor operation vs laparoscopic live donor nephrectomy*

|                             | Ratner et al <sup>13</sup> | Flowers et al <sup>14</sup> | Odland et al <sup>15</sup> | Wolf et al <sup>16</sup> |
|-----------------------------|----------------------------|-----------------------------|----------------------------|--------------------------|
| Open No.                    | 20                         | 65                          | 30                         | 10                       |
| Lap No.                     | 70                         | 70                          | 30                         | 40                       |
| <i>Parenteral analgesia</i> |                            |                             |                            |                          |
| Open                        | 12±88 mg MS                | 60.1 hours                  | 2.5±0.9 days               | 87±48 mg MS              |
| Lap                         | 40±33 mg MS                | 28.6 hours                  | 1.0±0.9 days               | 36±27 mg MS              |
| <i>LOS</i>                  |                            |                             |                            |                          |
| Open                        | 5.7±1.7 days               | 4.5 days                    | 3.8 days                   | 2.9±0.8 days             |
| Lap                         | 3.0±0.9 days               | 2.2 days                    | 2.7 days                   | 1.8±0.6 days             |
| <i>p</i> value              | 0.001                      | 0.0001                      | <0.05                      | <0.001                   |
| <i>Resume PO</i>            |                            |                             |                            |                          |
| Open                        | 2.6±1.0 days               | 51.0 hours                  |                            | 25±8 hours               |
| Lap                         | 0.8±0.5 days               | 16.3 hours                  |                            | 15±6 hours               |
| <i>p</i> value              | <0.001                     | 0.0001                      |                            | <0.001                   |
| <i>Resume full activity</i> |                            |                             |                            |                          |
| Open                        | 4.2±2.4 weeks              |                             | 25±9 days                  | 19.0±12.3 days           |
| Lap                         | 1.7±1.2                    |                             | 10±8 days                  | 9.9±5.0 days             |
| <i>p</i> value              | <0.001                     |                             | <0.05                      | 0.03                     |
| <i>Return to Employment</i> |                            |                             |                            |                          |
| Open                        | 6.5±3.1 weeks              | 51.5 days                   | 37±22 days                 | 29.1±11.3 days           |
| Lap                         | 4.0±2.3 weeks              | 15.9 days                   | 19±18 days                 | 24.4±12.2 days           |
| <i>p</i> value              | 0.003                      | 0.0001                      | <0.05                      | 0.42                     |

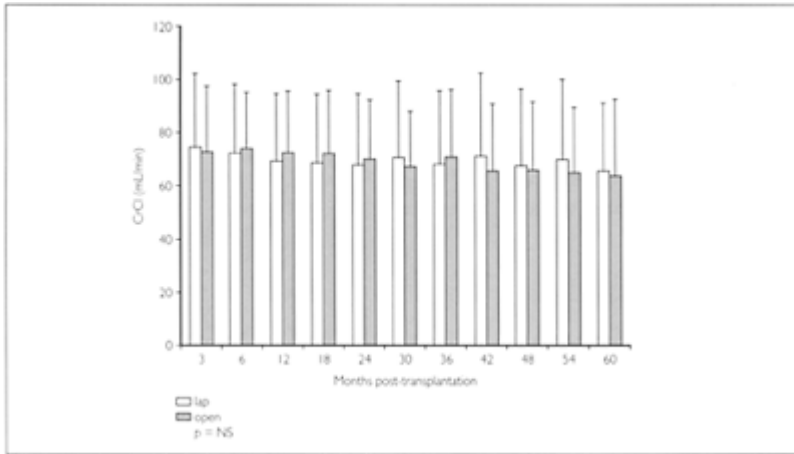
Open, open live donor operation; Lap, laparoscopic live donor nephrectomy.

to laparoscopic live donor nephrectomy, and Kuo et al have shown obese individuals to have similar outcomes to nonobese donors.<sup>22</sup> In a study that examined the demographic, radiologic, and anatomic factors that might affect the technical difficulty of laparoscopic live donor nephrectomy we found that none were predictive of how easy or difficult an individual's operation would be.<sup>23</sup> Obese patients were not any more likely to have technically difficult operations than thin patients.

Since laparoscopic control of venous bleeding may be difficult at times, it is often helpful to have a clear delineation of the renal venous anatomy preoperatively on imaging studies. Therefore, it is our practice that all live kidney donors undergo computed tomography (CT) angiography to ascertain the venous anatomy as well as the arterial anatomy of the kidney.<sup>24,25</sup> Magnetic resonance imaging (MRI) has also been shown to be useful for this purpose.

#### *Selection of the appropriate kidney and change in clinical practice*

Right laparoscopic live donor nephrectomy is more technically challenging than left, since the liver has to be retracted, and because the right renal vein is much shorter. Additionally, early reports noted a higher incidence of allograft thrombosis when the right kidney was procured laparoscopically,<sup>26</sup> although subsequent studies have



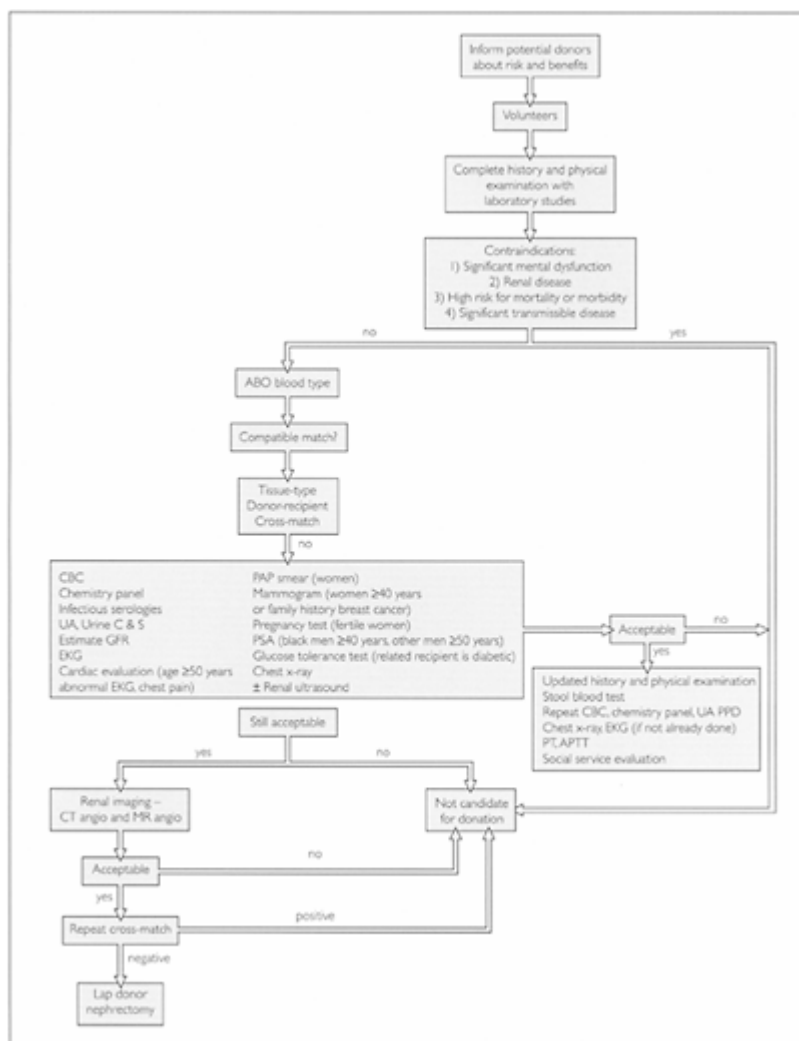
**Figure 12.1** Long-term renal allograft function is similar when comparing the recipient creatinine clearances of 381 kidneys procured laparoscopically vs 48 obtained from open donor nephrectomies via a flank incision.

shown that suitable recipient results can be achieved utilizing the right kidney.<sup>27,28</sup> Therefore, most surgeons will preferentially remove the left kidney laparoscopically for transplantation, even in the presence of multiple renal arteries or other vascular anomalies. This represents a significant change in practice compared to the open operation, where arterial anatomy usually dictated the selection of the kidney. With laparoscopic live donor nephrectomy, the majority of surgeons will reserve right nephrectomy for those cases where there is a disparity in the quality of the kidneys, so that the donor is left with the better kidney.

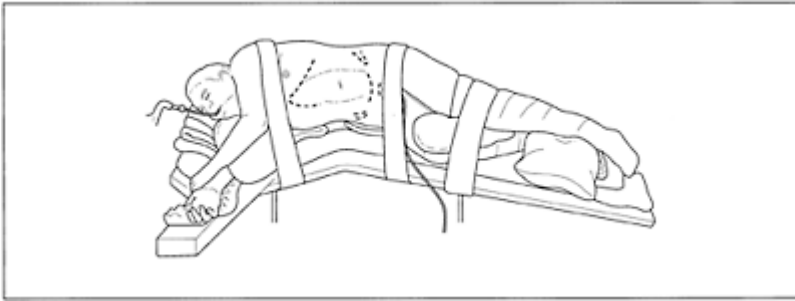
#### *Operative technique of laparoscopic live donor nephrectomy*

For a left donor nephrectomy the donor is placed in a modified right lateral decubitus position with the hips rolled posteriorly. After adequately securing the patient on the operating table (Figure 12.3), pneumoperitoneum is established via a Veress needle. Two 12 mm ports are placed in the abdomen, one at the umbilicus, and one slightly inferior to the umbilicus at the lateral border of the rectus abdominus muscle. A 5 mm port is inserted in the midline three-finger breadths inferior to the xiphoid. The videoendoscope is inserted through the umbilical port (Figure 12.4). The descending colon is then mobilized medially by incising the lateral peritoneal reflection. A 5 cm Pfannenstiel incision is made 2 cm superior to the pubis. A large 15 mm Endocatch bag is inserted through the Pfannenstiel incision through a purse-string suture in the peritoneum to maintain the pneumoperitoneum (Figure 12.5). The metal sleeve of the Endocatch bag

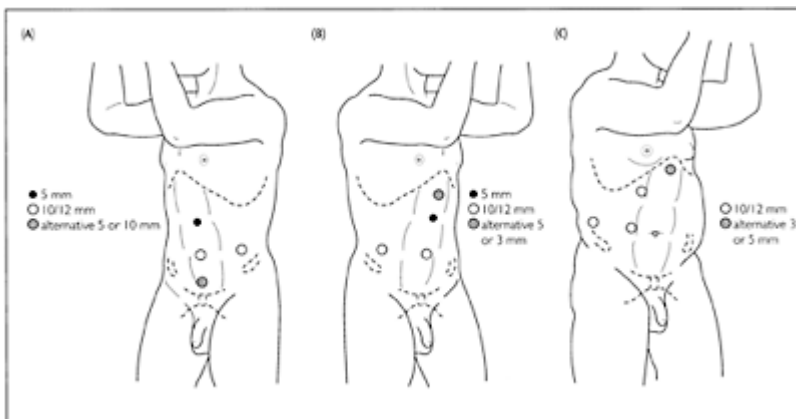
can then be used to retract the colon medially. Dissection is performed in the avascular plane between the descending colonic mesentery and Gerota's fascia until the gonadal vein is identified. The gonadal vein, ureter, and the lower pole of the kidney are all elevated anteriolaterally off the psoas muscle (Figure 12.6). The left renal vein is identified and dissected. Division of the lumbar vein off the posterior aspect of the renal vein gives exposure to the renal artery. The renal artery is dissected from the renal hilum to its origin at the aorta. The upper pole of the kidney is then freed from within Gerota's fascia and perirenal fat. The left adrenal vein is divided and the adrenal attachments to the left renal artery are also divided. The ureter and a generous mesoureter are then mobilized to the level of the iliac vessels and the gonadal vein is divided where it crosses lateral to the ureter. The inferior, posterior, and lateral aspects of the kidney are now freed. The ureter is divided approximately 12 cm distal to the lower pole of the kidney, after the distal ureter is occluded with hemostatic clips. At this point, the



**Figure 12.2** Flow chart for evaluation and clearance of potential renal donor

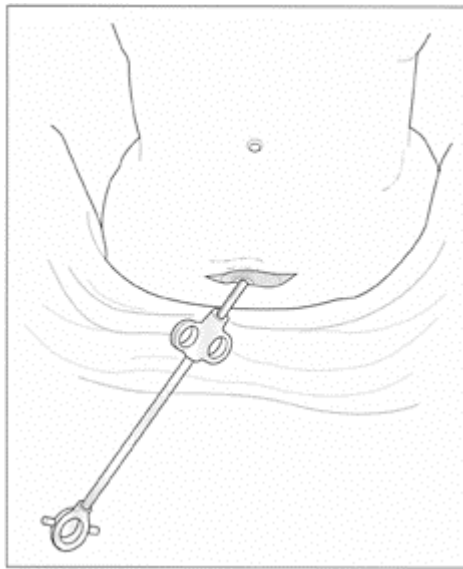


**Figure 12.3** Patient positioning and port placement for laparoscopic nephrectomy with autotransplantation. Similar positioning and port placement is employed for laparoscopic live donor nephrectomy, or native nephrectomy as an extirpative procedure. The patient is placed in a modified lateral decubitus position with the hips rolled posteriorly to allow easier access to the lower midline. The black dots represent the port sites. The kidney will be delivered through the Gibson incision that is marked on the patient prior to positioning, and then is utilized for the autotransplant.



**Figure 12.4** Trocar site placements.

Two 10/12 mm trocars are placed—one at umbilicus and one at the level of umbilicus lateral to the edge of rectus muscle. A 5 mm trocar is placed in the midline between the umbilicus and the xiphoid process. (A) Left-sided procedures; (B) right-sided procedures; and (C) in obese patients, all trocars are shifted laterally.



**Figure 12.5** An unopened Endocatch bag is inserted through a Pfannenstiel incision initially to retract the bowel medially when dissecting the renal vessels. At completion of the procedure, this device is utilized to entrap the kidney for removal.

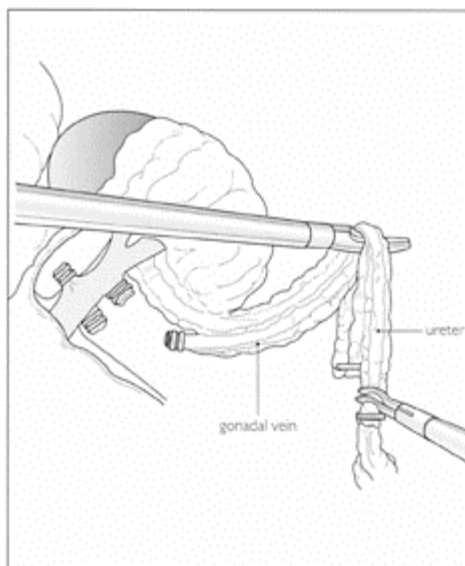
kidney is free from all attachments except the renal vessels.

The camera is switched to the left lower quadrant port. The renal artery is divided at its origin at the aorta with an Endo-GIA stapler passed through the umbilical port site (Figure 12.7A). After the renal artery is divided, the stapler is reloaded and used to divide

the renal vein in a plane medial to the adrenal vein stump in order to get maximal length of vein (Figure 12.7B). The kidney is placed over the spleen to allow space to deploy the Endocatch bag. Once deployed, the kidney is placed within the Endocatch bag and the kidney is retrieved via the Pfannenstiel incision.<sup>29</sup> Warm ischemic time is usually under 5 min.

### *Hand-assisted laparoscopic nephrectomy*

Laparoscopic donor nephrectomy requires considerable laparoscopic expertise to safely remove a kidney using only standard laparoscopic instrumentation. A number of authors have championed the use of hand-assisted tech-



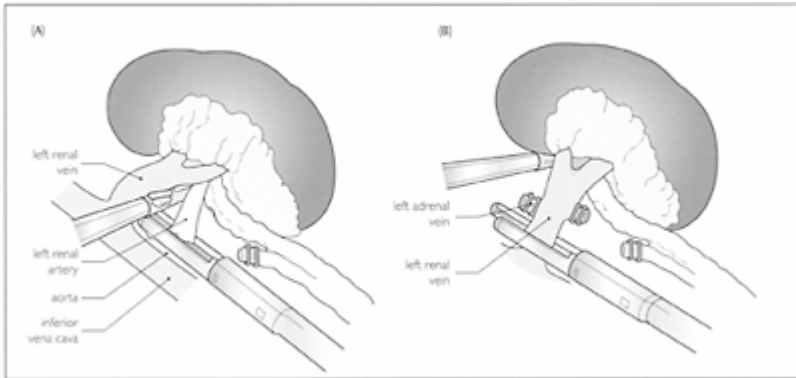
**Figure 12.6** The gonadal vein and ureter are dissected together to ensure the vasculature of the ureter.

niques for laparoscopic live donor nephrectomy.<sup>30,31</sup> The hand-assisted techniques allow less-experienced laparoscopic surgeons to perform laparoscopic live donor nephrectomies because a considerable portion of the operation can be performed bluntly with the intraperitoneal hand. The proponents of the hand-assisted technique also claim that there is a decrease in the operative time, that warm ischemic time can be reduced, and that it is theoretically safer, since the intraperitoneal hand can be employed to tamponade bleeding vessels while converting to an open operation in the case of a serious vascular injury.

A variety of commercially available hand-assist devices can be utilized. Additionally, the position of the hand port can be placed in a variety of locations depending on which hand the operative surgeon would prefer to have intraabdominal, whether the surgeon or

the assistant's hand is placed intra-abdominal, and which kidney is being procured. However, the most common position utilized for the hand port is probably either the periumbilical midline or the upper midline (Figure 12.8).

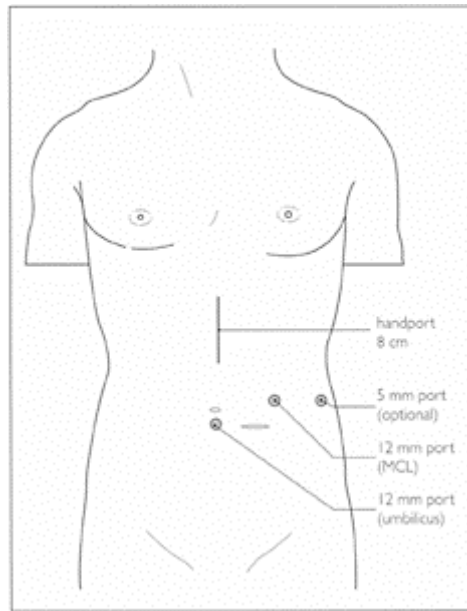
Compared to the open operation, hand-assisted laparoscopic donor nephrectomy appears to yield all the same donor functional advantages as the standard laparoscopic



**Figure 12.7A** The renal artery is divided at its origin of the aorta with a vascular Endo-GIA stapler.

**Figure 12.7B** The renal vein is divided in a plane medial to the adrenal vein to ensure maximum length.



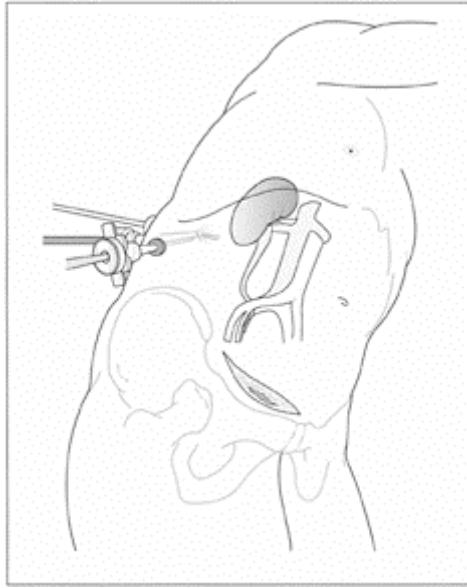


**Figure 12.8** Hand port and trocar placements for a right-handed surgeon for laparoscopic donor nephrectomy.

operation.<sup>32,33</sup> However, there has not been any randomized head-to-head comparison of the two laparoscopic techniques. In a recent survey of 130 transplant centers worldwide that perform laparoscopic live donor nephrectomy, we found a roughly even split between those centers that utilize the purely laparoscopic technique vs the handassisted technique.

#### *Retroperitoneal and gasless techniques (Figure 12.9)*

The majority of surgeons performing both the purely laparoscopic and the hand-assisted techniques of laparoscopic live donor nephrectomy employ a transperitoneal approach. However, the use of a laparoscopic retroperitoneal technique has been reported.<sup>34,35</sup> The advocates of this approach cite a procedure that more closely approximates the open operation performed via a flank approach and the theoretical lower risk of subsequent bowel obstruction by avoiding disturbing the integrity of the peritoneum. Several surgeons also utilize a gasless retroperitoneal approach that uses custom-built abdominal lifters for exposure. Few data demonstrating the results of these approaches have been published. The disadvantages of the retroperitoneal approach are that the operating space must be created by dissection and the operating space is generally limited.



**Figure 12.9** Trocar placements for retroperitoneal approach to laparoscopic donor nephrectomy.

*Concomitant surgery with laparoscopic live donor nephrectomy*

The transperitoneal laparoscopic approach to donor nephrectomy affords exposure to all quadrants of the abdomen with minimal need for additional incisions. Additionally, use of a Pfannenstiel incision to deliver the kidney provides excellent operative exposure for gynecologic or lower-tract urologic surgery. Molmenti and colleagues<sup>36</sup> have reported a series of concomitant operations with laparoscopic live donor nephrectomy which include laparoscopic adrenalectomy for adrenal incidentalomas detected on CT angiography, laparoscopic cholecystectomy, and bladder suspension for stress incontinence.

Gruessner<sup>37</sup> has also reported performing a concomitant laparoscopic live donor distal pancreatectomy with laparoscopic donor nephrectomy for a simultaneous live donor kidney/pancreas transplant. This was accomplished by using the hand-assist technique after making a supraumbilical 7 cm midline incision and using a HandPort System (Smith & Nephew). The kidney dissection and isolation from the surrounding structures was done in the usual fashion as has been described above. The dissection of the distal pancreas was begun in the inferior margin. The inferior mesenteric vein (IMV) was dissected and clipped. An avascular plane between the superior margin of the pancreas and the retroperitoneum was found and a small hole was made. A tunnel was then created behind the pancreas and a vessel loop was passed through for retraction of the pancreatic tail. The splenic artery and vein were dissected in the splenic hilum and clipped and divided. The rest of the intervening tissue between the pancreas and the spleen were divided with a stapler. After dissecting the splenic vein and artery right down to the

superior mesenteric vein (SMV) and celiac axis, respectively, the neck of the pancreas was circumferentially dissected free and heparin was given. The splenic vein was clipped close to its origin and the vein was clipped twice close to the portal vein and divided. The pancreas was stapled across and then removed and flushed. The patient had an uneventful postoperative course and was discharged home on day 6 after surgery.

### *Laparoscopic nephrectomy for renal autotransplantation*

Laparoscopic nephrectomy with subsequent open renal autotransplantation has been performed for a variety of pathologic conditions, which include proximal ureteral avulsion,<sup>38</sup> large mid-ureteral tumors,<sup>39</sup> hematuria-loin pain syndrome, and renovascular hypertension with multiple affected small renal arteries requiring bench surgery. Laparoscopic removal of the kidney for autotransplantation enables the open incision to be limited to the relatively minimal morbidity lower abdomen. The kidney can be delivered via the same incision that is utilized for the reimplantation.

### **Laparoscopic surgery in renal transplant recipients**

A variety of laparoscopic procedures have been reported in renal transplant recipients. The position of the renal allograft in either the right or left lower quadrant may limit laparoscopic port placement, and care must be taken to select appropriate locations for port placement to avoid injury to the allograft. Probably the most commonly performed laparoscopic operation in renal transplant recipients is the laparoscopic marsupialization and internal drainage of perirenal allograft lymphoceles, which is discussed below.

Laparoscopic surgery in renal transplant recipients offers several potential advantages that are specific to the immunosuppressed patient above and beyond the benefits that laparoscopy affords other patients in terms of decreased pain and quicker convalescence. First, it avoids the potential wound-related problems inherent in open surgery, which are particularly problematic in patients on long-term steroid therapy. Secondly, by reducing hospitalization, it reduces the risk for nosocomial infections. Thirdly, by allowing an earlier resumption of oral intake, it enables the continuation of oral immunosuppression.<sup>40</sup>

### **Laparoscopic internal drainage of lymphoceles**

Lymphocele formation is one of the most common complications after renal transplantation, with a reported incidence of 0.6–18% of cases.<sup>41–43</sup> The majority of these lymphoceles are small and remain asymptomatic. These fluid collections are identified on routine ultrasonography of renal allografts and, consequently, do not require therapeutic intervention. Symptomatic lymphoceles require intervention. Therapeutic possibilities include surgical peritoneal windowing, percutaneous drainage, and instillation of sclerosant.<sup>45–46</sup> Laparoscopic internal drainage of symptomatic lymphoceles has proven to be an effective therapeutic option, with decreased incidence of postoperative morbidity associated with open drainage procedures.

### *Clinical features*

Symptoms of lymphoceles include decrease of renal function (rise in serum creatinine) due to obstruction of the urinary tract, abdominal or perirenal discomfort or pain, swelling of the ipsilateral leg due to venous engorgement or thrombosis, edema of the external genitalia, change in micturition pattern, cutaneous lymph fistulas, infections such as pyelonephritis or cystitis, and unexplained weight gain. Rare complications include obstruction of the vena cava, arterial obstruction, or pulmonary embolism caused by iliac vein thrombosis.<sup>47–49</sup>

### *Diagnosis*

The diagnosis of a fluid collection around the renal allograft is made with ultrasonography or CT scan. It has been our experience that CT imaging is more useful than ultrasonography for planning subsequent surgery. Under ultrasound or CT guidance, the fluid can be aspirated and sent for bacteriological and biochemical analysis. The fluid creatinine is checked to rule out a urinoma. Lymphoceles are usually sterile, unless secondary infection has complicated the fluid collection. It is essential to distinguish a lymphocele from seromas, urinomas, hematomas, abscesses or homogenous tumor masses.<sup>50</sup> Renal angioscintigraphy can also be performed in order to rule out a urine leak.<sup>51</sup>

### *Management*

The treatment options for large symptomatic lymphoceles are varied. Percutaneous needle aspiration is the simplest approach, but the rate of recurrence is high (50–80%) and there is risk of secondary infection.<sup>41</sup> Aspiration of the lymphocele, along with injection of a tissue sclerosant (e.g. povidone-iodine solution, tetracycline), has a higher success rate.<sup>48,49</sup> Development of dense peritransplantation scar tissue after injection of the sclerosant may cause future problems because of the inflammatory response it produces. External drainage, via either surgically or percutaneously placed catheters, may have infectious or hemorrhagic complications. Recurrence rate is also unacceptably high (between 40 and 56%).<sup>52</sup>

Internal drainage has been considered the gold standard of lymphocele treatment since it was first described in 1966. A large peritoneal window along with marsupialization of the fluid-filled cavity is performed after an exploratory laparotomy. The fluid is allowed to drain freely into the peritoneal cavity from the retroperitoneal space, where the fluid is absorbed by the peritoneum. The advantage of the laparotomy is that it avoids potential complications such as vascular, ureteral, or bowel injury when the approach is retroperitoneal via the transplant incision.<sup>48</sup> Recurrence of the lymphocele (10–25%) usually occurs when the peritoneal opening is obstructed by the allograft kidney itself. In order to avoid this complication, a generous portion of the lymphocele wall must be excised<sup>49</sup> and the cavity can be reinforced with a piece of omentum.

The laparoscopic approach is now considered by many as the operation of choice for the definitive treatment of post-transplant lymphoceles. It has been found to be easy and safe<sup>48</sup> and efficiently drains the fluid without a formal midline laparotomy. It can be performed as an outpatient procedure, does not require any change in oral

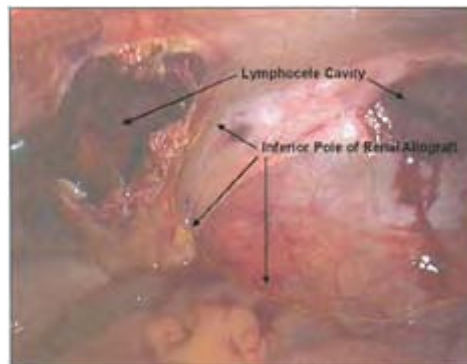
immunosuppression, and produces a better cosmetic result with less pain. An intra-abdominally placed pancreas graft is not a contraindication for this procedure.<sup>52</sup>

Most authors recommend that a laparoscopic approach be complemented with an intra-operative ultrasound for better localization of the fluid collection. Laparoscopic needle aspiration to confirm the site of the peritoneal window is performed to decrease vascular and ureteric complications.<sup>52</sup> Omentoplasty should also be performed.

There are some locations of the lymphoceles that may not be amenable to safe laparoscopic drainage. These lymphoceles are usually located lateral to the allograft. Such fluid collections will need to be drained by the open procedure. The author described a procedure of dual-scope laparoscopy to safely drain complex loculated lymphoceles by transilluminating the lymphoceles using two scopes.<sup>53</sup> Infected lymphoceles are also drained percutaneously and with antibiotic coverage.

### *Technique of laparoscopic drainage*

Under general anesthesia, an orogastric tube and a Foley catheter are inserted. Pneumoperitoneum is created with the Veress needle or by using the Hasson technique. After a pneumoperitoneum of 15 mm is achieved, ports are placed in the three quadrants that do not contain the allograft. A laparoscopic ultrasound can be used to localize the fluid collection or a bluish bulge in the peritoneum can be directly visualized. A needle aspiration is performed and fluid is sent for chemical and bacteriological examination. The hole in the lymphocele wall is then enlarged by sharp dissection using an endoscissors (Figure 12.10A). The cavity is then further visualized and the loculations are lysed. The fenestration within the peritoneum should be made as large as possible. Care must be taken to avoid injury to the allograft ureter, renal vessels, or native iliac vessels that may border the lymphocele cavity. Maximal fenestration can often be safely achieved by blunt dissection once an initial rent is made within the peritoneum. Hemostasis is achieved and the edges of the ellipse are secured with clips. If omentoplasty is planned, the edges of



**Figure 12.10A** The peritoneum, comprising the medial boundary of the lymphocele cavity, has been

fenestrated to allow easy drainage into the peritoneal cavity. The renal allograft can be appreciated adjacent to the lymphocele cavity.

the omentum are inserted into this cavity and clips or suture are used to secure its position in the lymphocele cavity<sup>52</sup> (Figure 12.10B).

### Laparoscopic cholecystectomy

Laparoscopic cholecystectomies are frequently performed in renal transplant recipients. The incidence of cholelithiasis is higher in the immunosuppressed patients than in the normal population.<sup>54</sup> This is particularly true in recipients who are immunosuppressed with cyclosporine,<sup>55</sup> a drug that is metabolized in the liver and excreted in bile. Although the exact mechanism is not known, cyclosporine has been shown to increase the lithogenicity of bile by altering bile salt-dependent and bile salt-independent flow in a dose-related manner. Also, patients who experienced persistent cyclosporine-related hepatotoxicity were more likely to form gallstones than those who suffered only isolated episodes.

Advantages of laparoscopic cholecystectomy include less postoperative pain, faster recovery, and the benefit of avoiding parenteral immunosuppression during the perioperative period.<sup>56</sup> Laparoscopic cholecystectomy can determine whether acute cholecystitis is the source of the fever or whether choledocholithiasis is the source of elevated liver function tests or the cause of pancreatitis<sup>57</sup> in an immunosuppressed transplant recipient. A recent case report demonstrated simultaneous islet cell transplant with laparoscopic cholecystectomy after extraperitoneal implantation of the allograft kidney.<sup>58</sup>



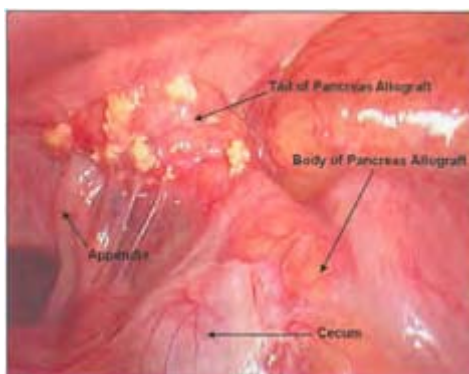
**Figure 12.10B** Omentum is inserted into the lymphocele cavity and sutured

to the peritoneal edge to prevent closure of the fenestration.

Technical considerations of laparoscopic cholecystectomy in the transplant patient are similar to those in the non-transplant patient with two exceptions. First, port placement must avoid injury to the allograft. This is generally not problematic, except perhaps in smaller patients. Secondly, patients on long-term steroid immunosuppression may have more friable tissues and must be handled more meticulously.

### Laparoscopic biopsy of kidney and pancreas allografts

Renal and pancreatic allograft biopsies are generally obtained by percutaneous techniques under ultrasound guidance. Complication rates range from 4 to 10%. However, a minority of patients may require the laparoscopic approach because the percutaneous approach is thought to be too risky because of clotting factor deficiencies or because the position of the allograft is such that there is a risk of damage to the surrounding structures. This is especially true in patients who have the intraperitoneal pancreatic allografts with portoenteric drainage<sup>59,60</sup> (Figure 12.11).



**Figure 12.11** Laparoscopic biopsy of pancreatic allografts can be performed safely when percutaneous access is difficult because of adjacent bowel loops. With enteric drainage of the pancreas exocrine secretions, the allograft is positioned with the duodenum oriented superiorly. The pancreatic allograft can be easily

visualized here with the adjacent structures.

### **Laparoscopic bilateral native nephrectomy following renal transplantation**

Unilateral or bilateral laparoscopic native nephrectomy can be performed following renal transplantation. The most common indications are refractory hypertension, or symptomatic autosomal dominant polycystic kidney disease. For the extirpation of small atrophic end-stage kidneys contributing to refractory hypertension, the laparoscopic approach can be performed safely and relatively easily via either a transperitoneal or retroperitoneal approach.<sup>61–63</sup>

Gill et al<sup>64</sup> have reported a 50% complication rate and prolonged operative times when laparoscopic bilateral nephrectomy is performed for large polycystic kidneys in renal transplant recipients. Our own enthusiasm for laparoscopic removal of polycystic kidneys in renal transplant recipients has also been tempered by a relatively high complication rate. Thus, although technically feasible, these cases should be approached with caution, particularly for extremely large kidneys.

### **Other laparoscopic procedures in renal transplant recipients**

There have been other case reports of laparoscopic procedures in patients who have received renal allografts. A case report from Fahlenkamp and associates<sup>65</sup> from Germany described the laparoscopic diagnosis and therapy of an undescended testicle in a 16-year-old renal transplant recipient. Another case report from Fedele et al<sup>66</sup> from Italy described the laparoscopic creation of a neovagina in a patient with Rokitsky syndrome who had also undergone a prior renal transplant.

### **Concomitant laparoscopic splenectomy and renal transplantation**

ABO blood group-incompatible live donor renal transplantation is being performed with increasing frequency. Single centers in Japan now have series in excess of 150 cases. Toma and colleagues in Tokyo<sup>67</sup> have reported longterm patient and graft survival rates following ABO-incompatible renal transplantation that are comparable with those achieved with ABO-compatible live donor transplantation. However, to achieve these results, the recipients must first undergo either plasmapheresis or immunoabsorption for acute removal of anti-A or anti-B blood group isoagglutinins and splenectomy at the time of transplantation to avoid antibody-mediated rejection that is difficult to treat and has historically had a high incidence of allograft loss.

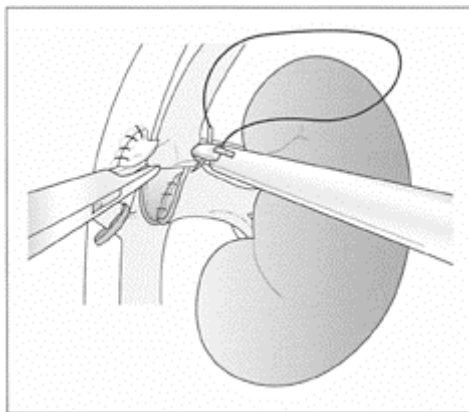
Laparoscopic splenectomy can easily be performed immediately prior to renal transplantation while awaiting the donor kidney. The spleen can be placed within an Endocatch bag and then be delivered through a small incision in the peritoneum when the Gibson incision is made for the renal transplant. Although no series of laparoscopic



splenectomies concomitant with renal transplantation have been published yet, a number of centers, including our own, are performing this operation for ABO-incompatible transplantation.

### **Laparoscopic renal transplantation (Figure 12.12)**

Now, with the advent of surgical robotics and improved laparoscopic instrumentation, it is likely that a laparoscopic recipient operation will soon be technically feasible. We anticipate that the renal transplant candidates most likely to benefit from a minimally invasive recipient operation will be obese individuals who are prone to wound complications with the open operation such as seromas, wound infection, dehiscence, and hernias. One technical consideration that will need to be addressed is how to keep the kidney cool while an intracorporeal anastomosis is being performed. In the near future we can expect to see both experimental and clinical series reported.



**Figure 12.12** Laparoscopic renal vein anastomosis during laparoscopic renal transplantation.

### **Conclusions**

Laparoscopy now plays an important role in renal transplantation. Laparoscopic donor nephrectomy has revolutionized the care of live kidney donors and has resulted in increased live donation rates. Similarly, a variety of laparoscopic applications have been applied to renal transplant recipients, resulting in the inherent advantages of shorter convalescence, less pain, and the ability to avoid complications unique to transplant recipients. In the future we expect to see broader application of minimally invasive procedures in transplant patients.

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## 13

# Minimally invasive treatment options for ureteropelvic junction obstruction

Debora K Moore and Robert G Moore

### Introduction

The treatment of ureteropelvic junction (UPJ) obstruction has been dramatically altered over the last two decades. Therapeutic options have been transformed from large open reconstructive operations to incisional endoscopic methods (endopyelotomy) or laparoscopic reconstructive procedures. These minimally invasive therapies have not only decreased hospital stay and postoperative narcotic usage but also have a shorter recovery time, while maintaining high therapeutic success rates.

### History and presentation

Ureteropelvic junction (UPJ) obstruction, which is usually the result of a congenital problem, can become symptomatic at any time. In neonates and infants, it is commonly associated with a palpable flank mass. With the advent of maternal ultrasonography, there has been a dramatic increase in the number of asymptomatic newborns being diagnosed with hydronephrosis and many of these infants are subsequently found to have UPJ obstruction.<sup>1</sup> UPJ obstruction has also been found during evaluation of azotemia, or incidentally found during contrast agent studies performed to evaluate unrelated anomalies such as congenital heart disease.<sup>2</sup> Older children or adults frequently present with intermittent abdominal or flank pain during periods of increased urine output, and at times these episodes are associated with nausea or vomiting. Hematuria, either spontaneous or associated with otherwise relatively minor trauma, pyuria, or frank urinary tract infection might also bring an otherwise asymptomatic patient to the attention of a urologist. Rarely, hypertension is the presenting finding.<sup>3</sup>

### Diagnostic studies

Excretory urography remains the cornerstone of radiographic diagnosis for ureteropelvic junction obstruction. Classically, radiographic findings on the affected side of a system with UPJ obstruction show a delay in function associated with a dilated pelvicaliceal system. The ureter, if visualized, should be of normal caliber, not dilated or narrowed. In

some patients, symptoms may be intermittent, and excretory urography between painful episodes may be normal. Therefore, the study should be repeated during an acute episode when the patient is symptomatic.<sup>4</sup> To better allow accurate diagnosis when using excretory urography, the patient should be well hydrated and receive an injection of furosemide, 0.3–0.5 mg/kg, intravenously at the time of the study.<sup>5</sup>

Diuretic renography with furosemide washout is the major study used to determine the presence or absence of a functionally significant obstruction.<sup>6</sup> The presence of medical renal disease, renal artery disease, or massive hydronephrosis may blunt the response of the kidney to furosemide or alter the dilution of the excreted radio—nuclide, thereby resulting in a false-positive study. On the other hand, a false-negative diuretic scan is rare; hence, if a normal curve is obtained, the system is probably not obstructed.

Knowledge of the presence or absence of a crossing vessel is very important for the choice of procedures to ensure successful repair of UPJ obstruction. Angiography, endoluminal ultrasound, and spiral computed tomography (CT) angiography have demonstrated great success in detecting a significant ( $>3$  mm) crossing vessel at the UPJ; their detection rates are 32%, 53%, 79%, respectively.<sup>7</sup> Overall, the incidence of crossing vessels at the UPJ ranges from 46%, as recorded at the time of open surgery, to 79%, with the use of spiral CT angiography in patients with obstruction. The collective incidence from several studies is approximately 50%, indicating a high prevalence of crossing vessels. The greatest problem with the presence of crossing vessels lies in determining whether it is etiologically or clinically significant.<sup>7</sup>

The use of magnetic resonance imaging (MRI) is of limited value in imaging intra-abdominal structures. The strength of MRI, however, is in providing detailed imaging of the vascular system and its physiologic information regarding renal blood flow and the functional status of the kidney. This information can be obtained in the azotemic patient without use of intravenous dye. Therefore, despite its limited role in the assessment of UPJ obstruction, it does have specific indications, particularly when associated with vascular disease (segmental crossing renal vessels) that is believed to be the cause of the difficulty.

Historically, the Whitaker test is the most invasive means of determining the presence or absence of functionally significant obstruction in the upper urinary tract. Compared with the diuretic renogram, the most common problem with the Whitaker test is that of a false-negative study and its often-indeterminate findings.

### **Etiology of UPJ obstruction**

Anomalies of the ureteropelvic junction may be classified as intrinsic, extrinsic, or secondary. An intrinsic lesion within the ureteropelvic wall may sometimes be the cause of obstruction, even in the absence of a gross anatomic cause. Murnaghan showed that there is an interruption in the development of the circular musculature of the ureteropelvic junction.<sup>8</sup> Hanna and associates, using electron microscopy to study UPJ obstruction, found that although the muscle cell orientation is normal, there is an excessive amount of collagen fibers and ground substance between and around the muscle cells; thus, muscle fibers are widely separated, and their points of connection are attenuated.<sup>9</sup> Congenital intrinsic narrowing or high insertion of the ureter into the renal

pelvis are common examples in this category. Less common causes of intrinsic UPJ obstruction include valvular mucosal folds, persistent fetal convolutions, and upper ureteral polyps.

The most common cause of extrinsic UPJ obstruction is an aberrant, accessory, or early branching vessel to the lower pole of the kidney. These vessels usually pass anteriorly to the ureteropelvic junction or upper ureter and have been suggested as a cause of obstruction. Stephens theorized that when an aberrant or accessory renal artery to the lower pole of the kidney is present and the ureter courses behind it, the ureter may angulate at two places: the ureteropelvic junction and the point at which it drapes over the vessel as the pelvis fills and bulges anteriorly.<sup>10</sup> Less commonly, a tissue band may cause extrinsic compression.

Causes of secondary UPJ obstruction are usually thought of as acquired anomalies. Included in this category are narrowings secondary to infection stones, urothelial tumors, inflammation, ischemia, and postoperative injury.<sup>11</sup>

### **Treatment options for UPJ obstruction**

Traditionally, open surgery has been the gold standard for treating UPJ obstruction, with a success rate over 90%.<sup>12–15</sup> Today, the minimally invasive options available for management of a patient with UPJ obstruction include balloon dilation, percutaneous antegrade endopyelotomy, retrograde cutting-wire balloon endopyelotomy, ureteroscopic retrograde endopyelotomy, transpelvic extraureteral endopyeloureterotomy, and laparoscopic pyeloplasty.

#### *Balloon dilation*

In 1982 Kadir et al initially reported on the use of balloon dilation using an antegrade approach.<sup>16</sup> Later, a retrograde approach, described by O'Flynn et al in 1989 as the 'Endobrst' technique, was introduced.<sup>17</sup> In this technique the dilating balloon is passed retrograde under fluoroscopic guidance and is used to rupture the UPJ. In 1997, Webber et al reported their 10-year experience using the retrograde approach.<sup>18</sup> Of the 55 patients that were evaluated, only 26 (34%) had improvement in their split renal function, drainage, or both. Thirty-two patients (42%) after a single dilation were pain free and, when combining single dilations with patients undergoing a second dilation, the painfree result only improved to 67%.<sup>18</sup> Despite being user friendly, because of its limited success rate, balloon dilation is not the mainstay of treatment for UPJ obstruction.

#### *Endopyelotomy*

Wickham is credited with performing the first percutaneous endopyelotomy in 1983 and, at the time, the procedure was referred to as 'pyelolysis'.<sup>19</sup> In 1986 the term 'endopyelotomy' was coined by Smith and associates when they reported their experience with this technique.<sup>20</sup> Endopyelotomy was developed based on the concept that smooth muscle regenerates around the incised ureteral segment during healing.<sup>21</sup> Since its inception, modifications of this approach have been made, including retrograde

approaches. Currently, various methods of incision have been tried and stent sizes and duration of stenting have varied—all remain controversial.

### Factors influencing endopyelotomy outcome

Prior to describing various incisional techniques, we will discuss both positive and negative predictors of endopyelotomy outcomes. Many investigators over the last two decades have published multiple articles demonstrating specific predictors of outcomes for incisional techniques for ureteral obstruction.<sup>22</sup> The predictors are outlined below.

**Length of obstruction.** UPJ obstructions with obstructed areas greater than or equal to 2.0 cm have a high rate of failure when treated endoscopically. These individuals warrant either laparoscopic or open reconstructive correction.<sup>23</sup>

**Presence of crossing vessels.** In 1994 Van Cangh et al<sup>24</sup> reported that the single most important factor determining a successful outcome for endopyelotomy was the absence of crossing vessels. A success rate of 42% vs 82% in the presence of crossing vessels was cited and preoperative evaluation was deemed essential to aid in treatment planning.

Subsequently, various modalities have been used to detect crossing vessels, including contrast-enhanced color Doppler imaging, endoluminal ultrasound (US), spiral CT angiography, or intra-arterial angiography with varying success.<sup>7,24–30</sup>

Investigators have reported that in adults with UPJ obstruction, 39% have a crossing vessel.<sup>24,30</sup> Quillen et al reported that, in their series, a significant vessel (2 mm or greater) was found in 38% of patients undergoing spiral CT angiography.<sup>30</sup> Bagley and Liu, using endoluminal US, found a crossing vessel in 52% of their patients.<sup>31</sup> Overall, the reported incidence of patients with crossing vessels and UPJ obstruction, as found by all modalities, is in the neighborhood of 50%.<sup>7</sup>

The effects of the crossing vessel on the obstructed UPJ surgical outcomes are controversial. Success rate for endopyelotomy among unscreened patients has been reported as >80%.<sup>7</sup> Gupta and associates found an apparent obstructing vessel in only 13 of 54 patients undergoing open surgery for failed endopyelotomy.<sup>32</sup> Nakada and associates used spiral CT to analyze the effects of crossing vessels on the results of fluoroscopic retrograde endopyelotomy and found crossing vessels present in 38% of patients who had a successful outcome.<sup>27</sup> In their study, the presence of a crossing vessel was associated with a reduction in success from 92 to 64%.<sup>27</sup> Clayman et al reported a >90% success rate in their hands when preoperative screening is performed and no crossing vessels are noted using a retrograde approach vs 64% when a retrograde approach is used with crossing anterior vessels identified.<sup>27</sup>

Currently, the appropriate preoperative screening for crossing vessels remains unclear. To date, no distinguishing features among patients with crossing vessels clearly preclude endopyelotomy. Size, number, location, and type of vessels in 'successful' endopyelotomies remain elusive. Sampaio supports the contention that the mere presence of a crossing vessel adjacent to the ureteropelvic junction does not imply that the vessel contributes to the obstruction.<sup>33</sup> He found an inferior polar artery crossing anterior to the UPJ in only 6.8% of cases. In only a few cases did these inferior polar arteries pass close to the UPJ. Thus, it appeared that anomalous arteries rarely caused UPJ obstruction. More commonly, an anterior crossing vessel was found in 65% in close proximity of the UPJ in



a normal kidney. In 26.7% of cases regarding the posterior surface of the UPJ, there was a vessel crossing at or lower than 1.5 cm above the posterior surface of the UPJ.<sup>33</sup>

The only notable recommendation was reported by Bagley and Liu,<sup>31</sup> who suggest refraining from endopyelotomy if anterior and posterior crossing vessels are simultaneously present, as, in their series, failure was 100% in both patients.<sup>31</sup> It was also reported that, with the use of endoluminal US, patients with loss of ultrasonic definition between mucosa and muscularis and who have dense fibrous tissue > 1 cm from the ureteral lumen tend to do poorly with endoscopic incision.<sup>31</sup>

It remains controversial whether or not it is necessary to diagnose crossing vessels before treating UPJ obstruction. However, endopyelotomy outcomes in the absence of a crossing vessel in combination with obstructed UPJ have been shown to have better outcomes. As in any procedure, thorough counseling of the advantages and disadvantages before therapy, along with a full knowledge of the patient's desires and expectations, remain key.

**Hydronephrosis.** High-grade hydronephrosis has a negative influence on the outcome of endopyelotomy.<sup>34–36</sup> Originally, Gupta and associates, upon reviewing their 401 percutaneous endopyelotomies, found that there was a highly significant correlation between the degree of hydronephrosis and the risk of failure of endopyelotomy.<sup>32</sup> Moderate hydronephrosis had a 96% success rate, while high-grade hydronephrosis had only a 50% success rate. Danuser et al went one step further and preoperatively calculated pyelocaliceal volume from the intravenous pyelogram radiographs and correlated these volumes to outcomes.<sup>37</sup> Pyelocaliceal volumes of <50 ml had an 87% success rate, volumes at 50–100 ml had an 81% success rate, while volumes >100 ml had a 69% success rate.<sup>37</sup> Van Cangh et al also found an inverse correlation with degree of hydronephrosis and success rate but added the absence/presence of crossing vessels into the equation.<sup>22,24</sup> They found that the risk of failure was as high as 95% for high-grade hydronephrosis in the presence of crossing vessels vs 39% failure rate for low-grade hydronephrosis with a crossing vessel.<sup>22,24</sup> Overall, patients with severe/ high-grade hydronephrosis have a significantly higher failure rate. The presence of crossing vessels appears additive. In the presence of severe/high-grade hydronephrosis, we recommend that reconstructive methods with renal pelvic reduction via either laparoscopic or open operative techniques be utilized.

**Renal function.** Renal function is a significant prognostic factor for endopyelotomy outcomes. Poor renal function (less than 20% differential function) is considered a relative contraindication to endopyelotomy.<sup>27</sup> Gupta and associates found that endopyelotomy was successful in only 54% (7 of 13 patients) with renal function less than 25%.<sup>32</sup> Shalhav and associates also found that when the affected kidney had poor function (14–25%), the success rate was 78%, whereas it was 85% in patients with moderate or good renal function (greater than 25%).<sup>38</sup> Danuser et al again confirmed the above findings. They found that primary UPJ obstruction treated with antegrade endopyelotomy failures had split renal function of  $33 \pm 13\%$  vs  $42 \pm 11\%$  for patients with successful endopyelotomy.<sup>37</sup>

In conclusion, reconstruction of the obstructed UPJ is recommended for the poorly functioning kidney.

**Primary vs secondary UPJ obstruction.** Originally, lessinvasive endopyelotomy procedures were reserved for treatment of secondary UPJ obstructions. Gupta and

associates found that patients with primary UPJ obstruction had a lower success rate of 82% than those with secondary obstruction (89%).<sup>7,32</sup> Recently, Matin et al reported that primary UPJ obstruction was associated with a higher symptomatic success rate of 68% for primary vs 50% success rate for secondary UPJ obstruction when performing laser endopyelotomy.<sup>39</sup> Their mean length of follow-up was a respectful 23.2 months (range 5–43 months) and, overall, they had a 65.4% symptomatic and 73.1% radiographic success rate.<sup>39</sup> Hoenig et al subgrouped secondary UPJ obstructions based on prior failed treatment and examined their subsequent endopyelotomy outcomes.<sup>40</sup> The secondary UPJ obstructions were divided into two groups: prior failed open pyeloplasty and prior failed endopyelotomy. Subjective outcomes were much higher for the failed open pyeloplasty group (88%) than the failed endopyelotomy group (71%). Moreover, objective successful outcomes were higher in the failed open pyeloplasty group (71%) than in the failed endopyelotomy group (55%).<sup>40</sup> Lastly, upon review of two of the larger and more recent laparoscopic pyeloplasty series looking at a combined 150 patients undergoing laparoscopic pyeloplasty, a significant decrease is seen in successful outcome in secondary vs primary UPJ obstruction (88 vs 98% and 75% vs 100%, respectively).<sup>41,42</sup> In conclusion, the published literature on this subject is not conclusive for primary and secondary UPJ obstruction as a predictor of outcome. One would intuitively reason that a primary obstruction would have the best chance of success vs a retreatment case with possible less vascularization and more fibrosis. Again, the patient's expectations need to be known upfront before pursuing one treatment modality over another.

**High vs dependent ureteral insertion.** Two groups have found that there was no statistically significant difference in success rates between the results of endopyelotomy in patients with a high ureteral insertion, UPJ obstructions with dependent ureteral insertion, and those with an equivocal insertion.<sup>43–44</sup>

**Renal calculi.** It is not uncommon to find renal calculi in association with UPJ obstruction. There is some controversy as to whether renal calculi result in UPJ obstruction or vice versa. Rutchik and Resnick recommend treating stones impacted at the UPJ primarily because the UPJ obstruction may resolve after successful treatment of the stone.<sup>45</sup> Also, they recommend that when UPJ obstruction is associated with a free-floating or caliceal stone, simultaneous stone removal and endopyelotomy should be done.<sup>45</sup> Jarrett and coworkers presented their experience with laparoscopic pyeloplasty plus pyelolithotomy in 20 renal units.<sup>46</sup> Before ureteropelvic junction repair, any stone was extracted through a laparoscopically made small pyelotomy incision that was eventually incorporated into the final pyeloplasty incision.<sup>47</sup> Stones in the renal pelvis were removed with rigid graspers under laparoscopic vision, whereas stones in the calices were removed via a flexible cystoscope introduced through a port. The renal pelvis was reconstructed based on the anatomy of the ureteropelvic junction. In their experience, 2 patients had residual calculi at postoperative follow-up of 3 months, giving a procedural stone-free rate of 90%. Overall longterm stone-free rate was 80% (16/20), as 2 patients had recurrent stones at mean follow-up of 12 months (range 3–57). Eighteen of the 20 cases (90%) had no radiographic evidence of obstruction.<sup>46</sup> Stasis due to upper tract obstruction may result in calculus formation but a minimally invasive approach to the obstruction may still be used and has no effect on success rate.

**UPJ obstruction and patient age.** Age is not an indicator for success. In fact, the overall success rate in the elderly has been reported to be comparable to that in younger patients and is as high as 88%.<sup>48,49</sup>

### Conclusion

Factors predisposing to failure or suboptimal outcome following an endourologic procedure have been examined. Factors that predict poor outcome or failure include significantly impaired ipsilateral renal function, massive hydronephrosis, and the presence of crossing vessels. Such entities cannot be corrected by an endourologic incisional approach and remain present after such attempts. In light of this knowledge, more definitive surgical treatment should be considered.

### Areas of controversy

Controversy continues in several areas of endopyelotomy: the method of incision, the size of stent after the endopyelotomy, and the stent indwelling time.

With an incisional method, a variety of apparently equally efficacious methods have been reported: coldballoon, dilating balloon, and the Ho: YAG laser. The knife, electrosurgical probe, electrosurgical cutting current results with any of these techniques appear to be similar.

Stenting practices seem to be driven by surgical experience and preference. No clear-cut proven approach to stenting practices has been elucidated and a complete discussion on stenting practices is beyond the scope of this chapter and therefore will be left to the discretion of the reader.

### Treatment modalities

#### *Percutaneous antegrade endopyelotomy*

Gupta and Smith of the Long Island Jewish Medical Center have the largest reported series of percutaneous endopyelotomies, performed over a 12-year period.<sup>32</sup> They found that 60 of 401 procedures failed, for an overall success rate of 85.0%.<sup>32</sup> The mean follow-up in this study was 51 months (range 6–144 months). Eighty-five percent of failures occurred in the first 6 months and 92% within 1 year postoperatively. Failures after 1 year were uncommon. They noted that most of the 60 patients who failed endopyelotomy underwent a successful open pyeloplasty, and endopyelotomy was successfully repeated in a few.

Percutaneous access is established similar to that for stone removal (see Chapter 29 for percutaneous nephrolithotomy or PCNL); however, for treatment of UPJ obstruction, access is obtained through an upper or midrenal calyx. This access allows a direct approach to the ureteropelvic junction. Current incisional devices that are available to incise the UPJ include the cold knife, electro surgical probe, electrosurgical cutting balloon, and laser energy. When thermal energy is used, the metal guide wire is protected by insulating it with an open-ended ureteral catheter. Typically, an incision is made in a

lateral position of the renal pelvis and carried 1 cm beyond the UPJ and up to about 2 cm into the renal pelvis. Under direct vision, a full-thickness incision is made until perinephric fat is visible. The advantage here is that because it is under direct vision, crossing vessels can be identified and avoided. If crossing vessels are incised at the time of incision, investigators report that the vessels may be easily and readily coagulated. Uncorrected bleeding diatheses and untreated infections are contraindications to percutaneous endopyelotomy, as is an anatomy unsuitable for percutaneous access.<sup>20,24,32,50</sup>

### *Retrograde ureteroscopic endopyelotomy*

Inglis and Tolley are credited with the first reported retrograde endopyelotomy using a diathermy hook passed through a ureteroscope to incise a strictured UPJ.<sup>51</sup> With the development of smaller-diameter rigid and flexible ureteroscopes and increased choices of devices for making a controlled incision, ureteroscopic endopyelotomy has gained in popularity.<sup>34–39,49,51–56</sup>

An initial retrograde may aid in delimiting the anatomy of the upper tract and define the area of obstruction. If a stent is not present preoperatively, the distal ureter may be calibrated with urethral catheters to 10F. If the ureter does not easily accommodate the catheters, a double pigtail stent may be placed and via soft dilation the case rescheduled in about 7 days' time.<sup>34</sup> Ureteroscopy using a 6F–8.5F semi-rigid ureteroscope is passed under direct vision to the level of the UPJ. A straight or angled tipped 2 or 3F electrocautery probe may be used with cutting current set at 40–60 W of pure cut. Minor bleeding can be handled by changing from cutting to coagulation mode.<sup>39</sup>

If laser energy is used, a 200 or 365 microfiber is available and the settings are 1.0–1.5 J, with a frequency of 12–15 pulses/s.<sup>39,53–55</sup>

An indwelling stent is placed at the end of the procedure for 4–6 weeks.<sup>34</sup> The incision is made in a lateral or posterolateral direction, beginning within the renal pelvis and extending across the UPJ into healthy tissue distal to the obstruction. To date, success rates with electrocautery or laser endopyelotomy appear similar.

Retrograde ureteroscopic endopyelotomy has similar success rates when compared to antegrade endopyelotomy. Meretyk and associates reported an overall success rate of 80% using a *retrograde approach*.<sup>52</sup> However, due to a 16% incidence of intraoperative hemorrhage and 10% incidence of distal ureteral strictures occurring postoperatively, this group abandoned the retrograde approach. It is believed that their ureteral stricture formation rate was secondary to the large-caliber rigid ureteroscopes and lack of prestenting. Gerber and Kim have presented their series with the longest follow-up mean of 29 months and, in their 18 primary and 4 secondary cases, a success rate of 82% was reported. No difference was seen in outcome when stent size postoperatively, incision type (cautery vs laser), or etiology of obstruction were compared. In their hands no bleeding or other serious complications were seen.<sup>56</sup> Thomas and associates reported the best success rates, at 94% in 49 patients (40 primary and 9 secondary), and low complication rates. In their series, mean follow-up was 15 months and they felt that their success was contingent upon if and only if a stent was placed 1 week prior to endopyelotomy.<sup>34</sup> It should be noted, however, that to date no other investigator has been able to duplicate their high success rate and we await long-term follow-up data.

*Retrograde endopyelotomy catheter (Acucise®)*

As originally described by Clayman, inventor of the Acucise®, this catheter was first approved for marketing by the Food and Drug Administration (FDA) in April 1993.<sup>57</sup> The advantage of this device is that it is positioned in a retrograde fashion under fluoroscopic guidance, negating the need for percutaneous access. The Acucise catheter is a cutting balloon catheter, 7F in diameter, that incorporates a monopolar electrocautery cutting wire and a low-pressure balloon. The size of the balloon varies between 4 and 10 mm. The balloon, itself, is used to define the area of stenosis and to carry the cutting wire into the area to be incised. The device has radiopaque markers on the catheter body at each end of the cutting surface, which provide reference points for positioning within the strictured area.

The Acucise device is passed over an 0.035-inch super stiff guide wire previously coiled within the renal pelvis.<sup>57-59</sup> While advancing the cutting balloon catheter, a side-arm adapter may be attached to the catheter and a retrograde ureterogram performed to define the area of stricture. Under fluoroscopy, the cutting balloon catheter is positioned over the guide wire so that the stricture/area of obstruction lies between the two radiopaque balloon markers. The investigators suggest that if one is unsure whether the balloon encompasses the stricture, the balloon can be gently inflated using 1 ml of diluted radiographic contrast; the demonstration of a waist with inflation of the balloon indicates that there is a narrowing or strictured area. The balloon is deflated prior to activation of the cutting wire. Contrast (0.5 ml) is injected into the balloon. The cutting wire is activated at 75–100 W (pure cut), while, simultaneously, another 1 ml of dilute contrast medium is instilled into the balloon. The mechanism of action for this technique is, basically, that as the balloon inflates, the cutting wire is advanced deeper into the ureteral tissue and the stricture is eventually incised. For treatment to be complete, the waist of the stricture should disappear and the balloon should appear to be fully inflated. The cutting wire is activated for only a few seconds, but if a waist is still present after instillation of 2 ml of contrast medium, the cutting wire may be reactivated for an additional few seconds. If the waist persists, then an alternative procedure for treating the stricture should be considered. If a longer incision is required, the balloon may be deflated and repositioned and the cutting procedure may be repeated. However, for strictures greater than 3 cm, it is recommended that a more definitive procedure using a reconstructive approach be utilized.<sup>57</sup>

Once the incision is complete, the balloon is deflated and the catheter is pulled distally. A retrograde ureterogram is performed through the Acucise balloon catheter to confirm extravasation at the incision site. After confirming adequacy of the incision, the balloon is repositioned across the incised area and fully inflated and the tamponade is maintained for 1–10 min. After the cutting balloon is deflated and removed, a 6–16F stent is placed over the guide wire. Stenting preference is based on the surgeon's preference and experience. A Foley catheter is placed to straight drain to monitor the patient for excessive bleeding or passage of blood clots, and by decompressing the bladder the risk of reflux is reduced. Typically, the ureteral stent is left in place for 2 days to 12 weeks postoperatively. Most investigators recommend leaving the stent indwelling for 6 weeks.<sup>57-59</sup>

Nadler and associates reported long-term follow-up (mean 33 months; range 24–43) of 28 patients who underwent Acucise endopyelotomy.<sup>58</sup> Diuretic renal scan showed

objective improvement in 81%. In the same group of patients, subjective analysis performed with analog pain scales showed that 61% of these patients had a favorable response, with 36% totally free of pain and 25% markedly improved.<sup>58</sup> Four patients (14%) failed, with mean time to failure of 7.8 months. Of the failures, 2 patients had successful repeat endopyelotomy and a single patient had a successful open pyeloplasty. Preminger and associates<sup>59</sup> reported a multicenter clinical trial using a cutting balloon catheter, in 66 patients with UPJ obstruction. The mean follow-up was 7.8 months and the overall success rate was 77% for endopyelotomy with a 72% success rate for primary UPJ obstruction vs a 100% success rate for secondary UPJ obstruction. Sharma et al reported on longterm outcomes for Acucise endopyelotomy for both primary and secondary UPJ obstruction in adults from a single institution. Fifty-four primary and 14 secondary UPJ obstructions were followed for an average of 6.1 years (range 0.7–10.1 years) after Acucise endopyelotomy. A success rate of 54% for primary and 50% for secondary UPJ obstruction was reported. In their experience, pretesting prior to therapy did not change success rate. They reported a complication rate of 15% for primary UPJ obstruction, with a 4% incidence of hemorrhage.<sup>60</sup> At the present time, unexpected late failures up to 5 years post-operatively for both antegrade and fluoroscopic retrograde endopyelotomy have been reported. Thus, we believe that all patients undergoing an incision technique to treat obstructed UPJ should be followed for a minimum of 5 years.

#### *Endopyeloureterotomy—transpelvic extraureteral approach*

In 1992 Ono et al, who developed a transpelvic extraureteral approach, reported their findings using this technique. For this method, a ureteral catheter or 0.038 inch guide wire is placed into the renal pelvis cystoscopically.<sup>61</sup> With the patient in the prone position, a percutaneous nephrostomy is established through one of the calyces to provide as straight a path as possible to the UPJ junction. The nephrostomy tract is dilated and a 28F Amplatz sheath (Cook Urological, Spencer, Indiana) is inserted. A nephroscope is inserted through the sheath, and under direct vision a 0.038 inch guide wire is passed down the ureter and into the bladder as a safety guide wire. A 22F urethrotome (Circon ACMI, Stamford, Connecticut) with a cold knife is inserted through the working sheath (Figure 13.1A-D). When the caliber of the ureteral lumen is normal, the ureteroscope can be easily passed through the distal ureter. The ureter is cannulated with a 6–16F percutaneous transhepatic cholangioscopy catheter (Sumitomo Behkurai, Japan) with the tapered end left in the distal ureter. Next, an 18–22F nephrostomy catheter is left in the renal pelvis. A nephrotomogram is performed through the nephrostomy catheter 3 weeks later. If no extravasation is observed, and the lumens of the UPJ and ureter appear to be adequate, the stent is removed. The nephrostomy catheter is clamped for 24 hours and if the patient remains asymptomatic it is removed.<sup>61</sup>

Recently, the investigators reported on the long-term follow-up of patients with UPJ or stenotic upper ureters using this novel technique.<sup>62</sup> A total of 127 procedures were performed in 123 patients with obstruction of the UPJ or stenosis of the upper third ureter. Mean follow-up was 58 months, with a range of 12–137 months. Therapy was considered successful if the patient was asymptomatic, when the degree of hydronephrosis improved on the postoperative excretory pyeloureterograms, and the renoscintigraphy revealed improvement of the half-time. Of the 107 cases involving UPJ

obstruction, 96 of these procedures (90%) relieved the obstruction and 11(10%) did not. The degree of hydronephrosis was rated as mild to massive, and again was correlated with success rate. In their experiences<sup>62</sup> success rate did not differ significantly between the four grades of hydronephrosis. The success rate when comparing primary to secondary obstruction was not statistically significant in their series. Of the 47 cases in which the stenotic segment was 2 cm or greater in length, 43 patients (91.5%) had alleviation of the obstruction and 4 (8.5%) did not. In the 80 cases where the stenotic segment was less than 2 cm in length, 72 cases (90%) relieved the obstruction and only 8 (10%) did not.<sup>62</sup>

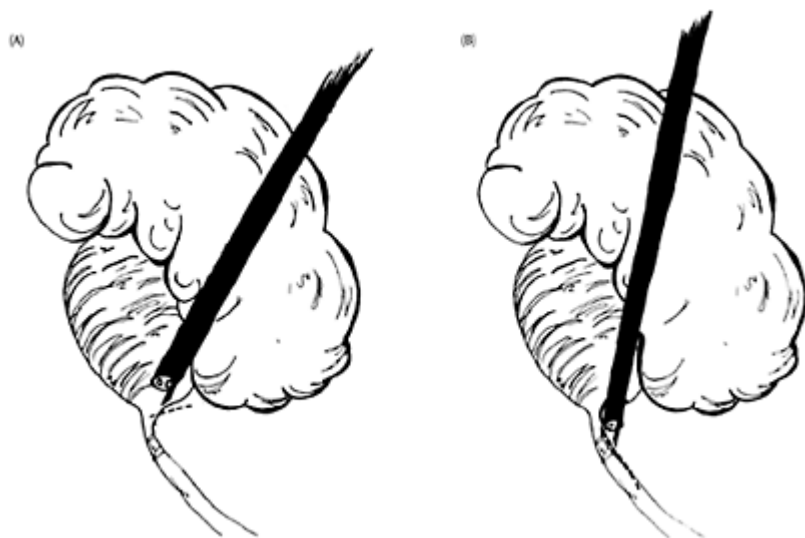
In keeping with other reports when kidney function was factored into account, the success rate in 7 patients with a diseased kidney that contributed less than 25% of total function was 57% as compared to a 92.5% success rate in 120 patients with renal function at 25% or greater.<sup>62</sup>

Failure occurred in 5 patients. The reported time to recurrence was 1 year in 3 patients, 2 years in 1, and 4 years in another patient. Two of the 5 patients were treated successfully with percutaneous endopyelotomy. One patient underwent nephrectomy due to kidney dysfunction and another patient is under observation. The remaining patient was lost to follow-up.<sup>62</sup> Their operative complications included fever (>38°C for more than 2 days) in 12 (9%), temporary hematuria in 3 (2%), and prolonged hematuria caused by a pseudoaneurysm and pneumothorax in 1 patient each. Four patients required 1–3 units of blood (3%).<sup>62</sup>

This single institution report using this novel technique has very impressive results; however, without validation from other investigators, the true benefit of this technique is yet to be realized.

### *Conclusion*

Endopyelotomy, regardless of methods of incision or approach, has been successful. However, the overall success rates do not approach those with laparoscopic or open pyeloplasty (95–100%)<sup>12–15,37,38</sup> Recent long-term outcomes studies by Sharma and Strem have shown successful outcomes (50–54%) to be much less than previously reported by Smith and Gupta.<sup>32,60,63</sup> This necessitates the need for endopyelotomy centers to publish their long-term outcomes studies. However, until this takes place, patients should be counseled accordingly about the potential decreased long-term success of endopyelotomy. Nevertheless, postoperative morbidity and recovery time have decreased and improved for endopyelotomy compared to open pyeloplasty. Complications have been relatively few, with bleeding requiring transfusion reported in 1%–9% of patients.<sup>64–67</sup> The overall major complication rate reported is approximately 11%. Serious complications include ureteral



**Figure 13.1** An endopyelotomy-transpelvic extraureteral approach. (A) The pelvic wall is incised 1–1.5 cm from the UPJ junction, with the incision extending toward the renal parenchyma. (B) Through the incision, the ureterotome is then advanced into the retroperitoneal space. (C) The incised end of the UPJ or the dilated ureter is visualized in the retroperitoneal space.

avulsion, ureteral necrosis, and arteriovenous fistula formation.<sup>64–67</sup> Complications rarely reported include urinoma, hematoma, and urinary tract infection.

### *Laparoscopic pyeloplasty*

Open pyeloplasty is the gold standard for correction of UPJ obstruction. Success rates following open pyeloplasty in contemporary series are greater than 90%.<sup>12–15</sup> However, postoperative morbidity associated with open renal surgery causes significant pain and a prolonged convalescence from the flank incision. In an attempt to decrease morbidity, a less-invasive alternative, laparoscopic pyeloplasty, was developed to reconstruct the obstructed UPJ.

Laparoscopic pyeloplasty was first reported in 1993 by two groups, Schuessler et al and Kavoussi et al.<sup>67,68</sup> In these early cases, the stented dismembered pyeloplasty technique was utilized. Since the inception of laparoscopic pyeloplasty, dismembered and



flap-type procedures have been reported via both transperitoneal and retroperitoneal approaches.<sup>12,41,42,68–77</sup>

Laparoscopic pyeloplasty may be offered to most patients with UPJ obstruction, including those who have failed endopyelotomy and open pyeloplasty. Patients who are considered unsuitable for endopyelotomy due to crossing vessels, massive hydronephrosis, or anatomic abnormalities such as horseshoe or pelvic kidneys are ideal candidates for the laparoscopic procedure. Relative contraindications such as a small intrarenal pelvis or a history of previous open pyeloplasty complicated by undrained urinoma are appropriate for beginning laparoscopic surgeons but are not necessarily contraindicated for the experienced laparoscopist.

A retrograde pyelogram which defines both ureteral and renal pelvic anatomy aids in ruling out urinary collecting filling defects and stones, characterizes the ureteral-pelvic insertion, confirms the length of the UPJ stricture when dealing with secondary obstructed UPJ, and demonstrates the size of the renal pelvis. Using a retrograde pyelogram, information is gathered for appropriate operative planning (i.e. reduction of renal pelvis, type of flap planned, and/or endoscopic stone extraction via the pyelotomy incision prior to reconstruction).

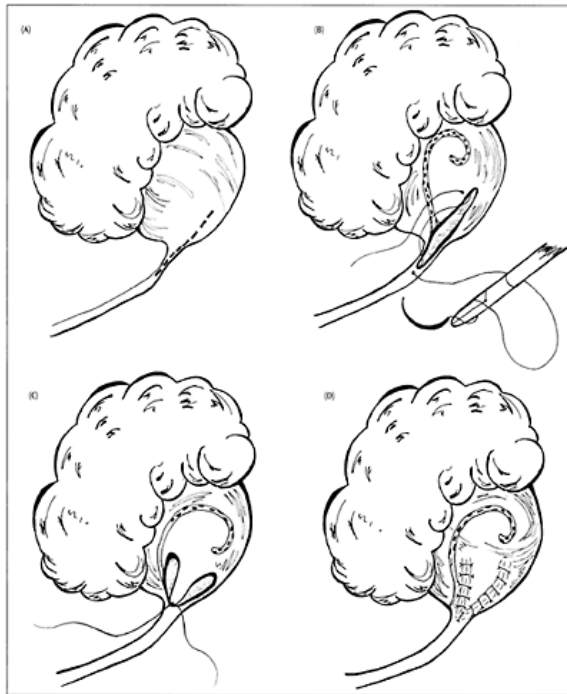
Chronic indwelling ureteral stents placed to alleviate UPJ obstruction-induced flank pain are optimally removed more than 1 week prior to laparoscopic reconstruction. Removing the stent in a timely manner facilitates a reduction in periureteral edema at the time of laparoscopic reconstruction and in turn optimizes suture placement and knot tying with the goal of achieving a tension-free watertight anastomosis. Outcome analysis for laparoscopic pyeloplasty in which chronic indwelling stents are left in place up to the time of surgery report longer operative times than laparoscopic repairs involving primary and secondary obstruction without chronic stenting. Chronic stenting also resulted in longer hospital stays and higher use of pain medication in this group. Not surprisingly, the success rate was reduced in patients with chronic indwelling stents when compared to patients that did not have chronic indwelling ureteral stenting in place prior to repair.<sup>75</sup>

### **Laparoscopic pyeloplasty technique**

Typically, laparoscopic pyeloplasty is performed through a transperitoneal approach, as the peritoneal cavity provides adequate space for intracorporeal suturing. The initial step is cystoscopy, retrograde pyelogram, and placement of an indwelling ureteral stent in the upper pole caliceal system. The curl of the stent is positioned away from the area to be newly reconstructed, commonly in an upper pole calyx to optimize a watertight anastomosis. Positioning of a stent at the UPJ will make subsequent suture placement difficult; therefore, a ureteral stent that is 2 cm longer than measured is utilized. The patient is positioned in the modified 45° lateral decubitus position. A 3 or 4 port access technique is utilized. A 10/12 mm periumbilical trocar is used for the videoendoscope (30° and/or flexible tip). Secondary/working trocars for intracorporeal suturing are either placed in the midline (one 8 or 10/12 mm trocar in the upper midline and one 8 or 10/12 mm trocar in the lower midline) or in the triangular configuration (one 8 or 10/12 mm in the upper midline and one 8 or 10/12 mm in the mid-clavicular line at the level of the umbilicus). A lateral anterior axillary line 5 mm trocar is placed at the level of the

umbilicus after reflection of the colon. The procedure is performed at ease when the surgeons are able to place and tie sutures with either hand.

For a transperitoneal approach, the colon is reflected and the ureter is identified. The ureter travels parallel and posterior to the gonadal vessels as it transverses the psoas muscle. To facilitate identification of the ureter, the gonadal vessels are retracted anteriolaterally. The ureter is traced proximally until the renal pelvis is identified. The ureter just below the UPJ and renal pelvis are mobilized from surrounding tissue/structures with the aid of a harmonic scalpel. Overzealous dissection of the proximal ureter is avoided, so the segmental vascular supply remains intact. If crossing vessels are not present, any number of flap procedures can be performed. If anterior crossing vessels are encountered, they are dissected away from the UPJ and/or renal pelvis. Again, the entire renal pelvis is mobilized from surrounding tissue anteriorly, posteriorly, and medially. This step is especially important when a reduction pyeloplasty is being considered. The UPJ is incised circumferentially on the renal pelvis side. Here,



**Figure 13.2** Non-dismembered pyeloplasty. (A) Using a laparoscopic knife, a medial incision is made from 1.0 cm above the UPJ. This incision is taken down the medial side of the ureter for 1.0–1.5 cm. (B and C) The

mid-portion of the upper flap is sutured down to the apex of the ureterotomy with an interrupted 4–0 absorbable suture. (D) The remaining part of the anastomosis on the left and right of the central sutures is closed with a 4–0 absorbable suture.

care must be taken so as not to inadvertently cut the previously placed ureteral stent. The ureter and pelvis are transposed so that the opposite sides of the vessels lie behind the renal pelvis. Alternatively, the crossing vessels can be repositioned cephalad away from the point of obstruction and fixed by intracorporeal sutures.<sup>76</sup>

Repositioning the vessels resolves the extrinsic obstruction; however, it will not address any intrinsic component of obstruction. If a posterior crossing vessel is identified, a laparoscopic non-dismembered pyeloplasty may be performed (Figures 13.2A–D). As in open cases, the cut end of the ureter is spatulated posteriolaterally for 1.0–1.5 cm (Figures 13.3A,B). Sutures are placed using 4–0 absorbable sutures either in a free hand, intracorporeal manner, or using a semi-automated suturing device (Endostitch; USSC, Norwalk, Connecticut). Note that in 1998, Chen et al reported that because of the large-diameter needle, as used in the Endostitch device, leakage may appear and such leakage leads to increased potential for fibrosis and to eventual failure of the repair.<sup>71</sup> Furthermore, Turk et al suggest that instead of using such a device, the less-experienced laparoscopist use a straight needle for intracorporeal suturing. The skilled surgeon will find no difference in using either a straight or curved needle; we suggest use of either an SH or an RB-1 needle.<sup>78</sup>

The first suture is placed at the most dependent portion of the renal pelvis through the corresponding apex of the laterally spatulated ureter (see Figure 13.3B). Sutures are placed such that tied knots are outside the urinary tract to prevent urine-induced stone formation on the suture. The posterior aspect of the ureteral-renal pelvic anastomosis is then performed using either multiple interrupted sutures or with a running suture (Figure 13.3C). Passing the apical stitch under the new anastomosis facilitates exposure of the posterior portion of the anastomosis. The anterior portion of the ureteral-renal pelvis is completed in similar fashion. The posterior suture is passed through the anterior portion of the renal pelvis near the newly completed ureteral-renal pelvic anastomosis and tied to the end of the anterior running suture. After completion of the ureter to the renal pelvis, redundant renal pelvis tissue is resected (reduction pyeloplasty; see Figure 13.3D). The remainder of the pyelotomy incision is closed from the upper portion of the pyelotomy incision, running down toward the ureteral anastomosis.

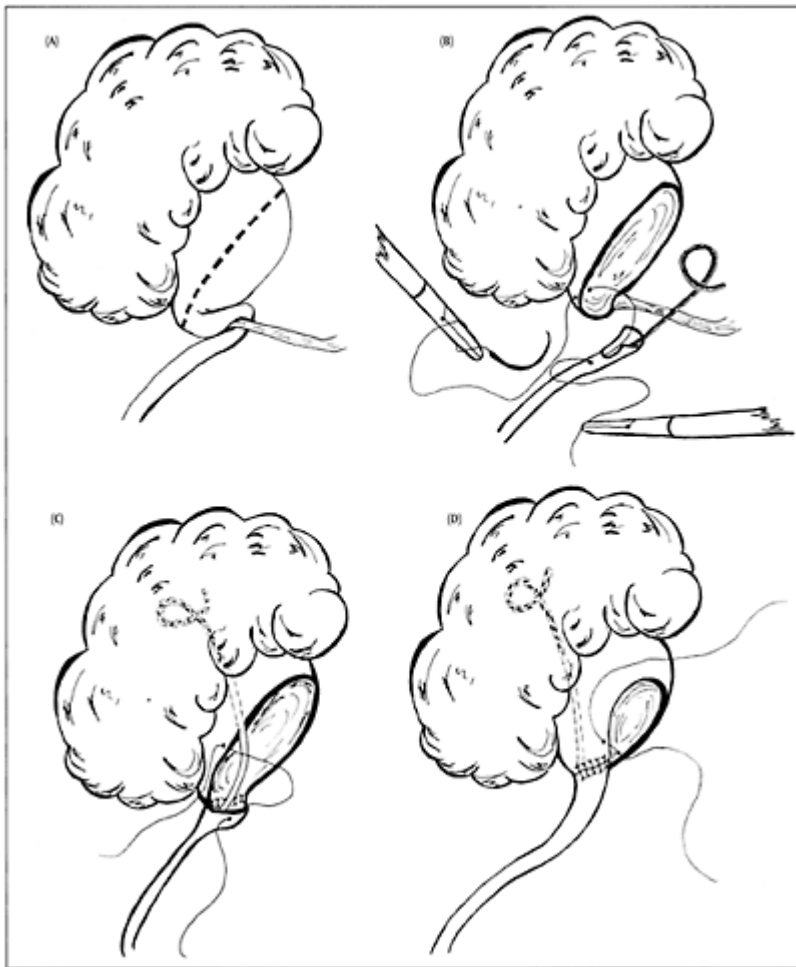
### **Retroperitoneoscopic technique**

Less experience and shorter-term follow-up are available for the retroperitoneoscopic pyeloplasty. Theoretically, intracorporeal suturing is more complex secondary to the smaller operative space of the retroperitoneum by those not accustomed to a retroperitoneal approach. Again, an operative approach is based on surgeon

experience/preference. A double pigtail ureteral stent is placed as previously described. The patient is positioned in the 90° flank position without overextension. An incision is made in the lumbar triangle between the 12th rib and the iliac crest over the latissimus dorsi muscle. A tunnel is created through the flank muscles until the retroperitoneal space is entered. Using the index finger, the peritoneum is pushed anteriorly toward the midline. Two 5 mm trocars are placed in the anterior and posterior axillary line, respectively. Two additional 5 mm trocars are placed at Petit's triangle and the intersection of the 12th rib and paraspinous muscle. A 10/12 mm trocar is placed at the site of the original incision.<sup>42,74,78,79</sup> The camera port is placed as the most dependent trocar.

Initially, the incision starts at the posterior edge of Gerota's fascia and the stented ureter is identified after anteriomedial retraction of the kidney. Both the ureter and renal pelvis are freed from surrounding structures/ tissues. Two nylon stay sutures are inserted transcutaneously with a straight needle to place the renal pelvis on stretch. This maneuver adequately exposes both the renal pelvis and UPJ, allowing for unimpeded circumferential incision of the UPJ on the renal pelvic side. The redundant pelvis is reduced and aberrant crossing vessels are transposed. Interrupted or running 4-0 Vicryl sutures are utilized to complete the ureteral-renal pelvic anastomosis in a similar fashion to that described for the transperitoneal approach.<sup>75</sup>

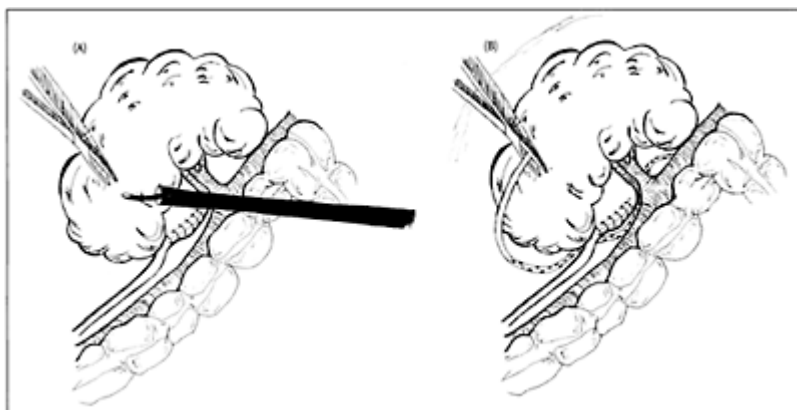
After completion of the pyeloplasty, a closed suction drain is placed intra-abdominally via the most lateral laparoscopic port (Figure 13.4A,B). But if the procedure has been performed transperitoneally, some investigators recommended that the drain be extraperitonealized. A Foley catheter drains the bladder for 1 to 2 days postoperatively. A creatinine level measurement is performed on the drain fluid. If the laboratory results are elevated, suggesting a urine leak, the drain is continued and creatinine levels are checked again when the drain output drops. If the drain output increases after the Foley catheter has been removed, the Foley catheter should be immediately replaced to eliminate reflux via the stent in the recently treated ureter and therefore decrease the chances of extravasation. The ureteral stent placed intraoperatively is removed after about 1 month for primary UPJ obstruction with a normally functioning kidney. For secondary UPJ and/or marginally functioning kidney (split renal function of <35% on renal scan), the ureteral stent is left indwelling for 1.5–2.5 months. Complications have included transient ileus, thrombophlebitis, bleeding requiring transfusion (0–3%), or urinary leakage. In the Hopkins series, 11% of the 100 treated patients developed complications.<sup>41</sup>



**Figure 13.3**

Dismembered pyeloplasty. (A) The area of UPJ obstruction is excised and sent to pathology. The ureter is spatulated laterally for 1.0–1.5 cm. (B) The cut end of the ureter with proximal end of ureteral stent is brought anterior to the crossing vessel. The most dependent area of the renal pelvis is sutured to the apex of the spatulated ureter. All knots are placed so that the

tied knot will be on the outside of the ureter. (C) The posterior area of the anastomosis is closed using 4–0 absorbable sutures. (D) The anterior portion of the anastomosis is closed utilizing 4–0 absorbable sutures in an interrupted or running fashion. The remaining renal pelvis is reduced and closed in running fashion.



**Figure 13.4** Laparoscopic drain placement (A and B). A laparoscopic grasper is used to introduce a 19F round drain through the mid-clavicular 12 mm trocar. The end of the drain is occluded to prevent air loss. Using a curve-tipped grasper placed through the anterior axillary trocar, the tip of the drain is cannulated and grasped and withdrawn through the most posterior trocar. The end of the drain is positioned by the newly repaired UPJ but not in direct contact. The posterior trocar is removed and the drain is sutured to the skin.

For results see Table 13.1.

In Schuessler's initial report on 5 patients, complete resolution of symptoms was achieved in all patients at a mean follow-up of 12 months.<sup>67</sup> The main advantages of their procedure over open operative intervention were shorter hospital stay, averaging 3 days, and return to routine activities within 1 week. In a 1995 comparison for treatment of the UPJ obstruction, Brooks et al reported on 12 patients that underwent a laparoscopic approach, which like their open counterparts, was 100% successful.<sup>12</sup> However, operative time for laparoscopic approach was prolonged when compared to the open counterparts. Later, Bauer et al compared objective and subjective outcome of open versus laparoscopic pyeloplasty.<sup>73</sup> In this report pain relief, activity level, and relief of obstruction outcomes were equal in both the laparoscopic and open approach. Recently, the Hopkins group reported on their first 100 laparoscopic pyeloplasty cases.<sup>41</sup> Since 1995, operating time has decreased as skill level has increased. Importantly, this report confirmed that not only was the laparoscopic approach as successful as the open procedure but also that it was as durable as the open approach. With a mean clinical and radiographic follow-up of 2.7 and 2.2 years, respectively, 96% of the 100 patients were free of obstruction on follow-up radiographic imaging (see Table 13.1). In this series, all failures occurred within the first postoperative year.<sup>41</sup> Obstruction persisted after laparoscopic pyeloplasty in 4 of the 100 patients. Of these 4 patients, 2 patients eventually developed atrophic kidneys, with one requiring a laparoscopic nephrectomy. The remaining 2 patients have prolonged half-time on renal scan and are being followed.<sup>41</sup>

Today, numerous laparoscopic centers offer a laparoscopic approach for treatment of UPJ obstruction. At these centers laparoscopic pyeloplasty has rapidly become the 'standard of care' for the treatment of the obstructed UPJ. However, before it becomes mainstream, one needs to remember that the retroperitoneal approach currently has only short-term follow-up, and, while long-term outcomes are pending, similar outcomes to the transperitoneal approach are expected.

**Table 13.1** *Results of management of UPJ obstruction*

| Investigator                   | No. of procedures | Approach | No. dismembered | Mean OR time      | Open conversion | Hospital stay (days) | Complications    | Success | 1   | 2       |
|--------------------------------|-------------------|----------|-----------------|-------------------|-----------------|----------------------|------------------|---------|-----|---------|
| Sla ma et al <sup>79</sup>     | 15                | R        | 7               | 178 min (100–250) | yes 1/15        | 4.8(1–14)            | post op 3 (21%)  |         |     |         |
| Eden et al <sup>42</sup>       | 50                | R        | 50              | 2.45 h            | 2 (4%)          | 2.6 (2–7)            | yes 2            | 96      | 100 | 75(3/4) |
| Soulie et al <sup>80</sup>     | 55                | R        | 48              | 185 min (100–260) | 5.4%            | 4.5(1–14)            | 7/55=12.7%       | 88.9    | NA  | NA      |
| Jarrett et al <sup>41</sup>    | 100               | T        | 71              | 4.2 h (2–8)       | 0               | 3.3(2–8)             | Yes              | 96%     | 98% | 88%     |
| Turk et al <sup>78</sup>       | 49                | T        | 49              | 165 min (90–240)  | 0               | 3.7(3–6)             | Yes (1/49)       | 97      | 97  | NA      |
| Siqueira et al <sup>81</sup>   | 19                | T        | 16              | 240 min (128–470) | 0               | 2.9 (2–7)            | Yes (2/19) 11.7% | 91.7    | 100 | (7/9)   |
| Pardalidis et al <sup>82</sup> | 8                 | T        | 8               |                   |                 | 3.5                  | 5 (4–12)         | 100     |     |         |

|                                 |     |   |     |   |     |     |  |
|---------------------------------|-----|---|-----|---|-----|-----|--|
| Baldwin<br>et al <sup>83</sup>  | 17  | T | 16  | 3.3 h; last<br>5<br>procedures<br>2.8 h | 1.4 | No  | 94   |
| Klingler<br>et al <sup>84</sup> | 40  |   | 25  |   |     | 5.9 | 96<br>dismembered<br>11/15 non-<br>dismembered |
| Total                           | 303 |   | 240 |   |     |     |  |

Key: OR, operating room; R, retroperitoneal; T, transperitoneal

## Conclusion

Minimally invasive operative techniques to treat the obstructed UPJ have been accepted within the mainstream of the urologic community. All types of endopyelotomies are commonly performed by the community urologist. Although laparoscopic reconstructive techniques are not routinely performed by the average private practice urologist, this treatment modality is becoming routine in most academic centers. Some authors have recently reported lower than expected long-term outcomes (50% vs 85%) with endopyelotomy techniques.<sup>32,60,63</sup> More longterm investigations on the outcomes of endopyelotomy by other centers need to be examined; until this take place, both results need to be discussed with prospective operative candidates given that only one long-term follow-up for post-laparoscopic pyeloplasty has been published with results that mirror long-term outcomes for open pyeloplasty (>90% success rate).<sup>41</sup> Patients are the biggest advocates of minimally invasive treatment of the UPJ and this is the major driving force behind the direct infusion of the techniques in the general urology field.

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## 14

# Minimally invasive therapies for renovascular hypertension disease

Alan Lumsden and Ramesh Paladugu

### Introduction

Renovascular hypertension (RVH) represents a pathophysiologic condition in which elevated systemic blood pressure is caused by renal artery occlusive disease. RVH has become increasingly recognized as an important cause of clinically atypical hypertension and chronic renal failure since Goldblatt's seminal experiment in 1934. RVH is the clinical consequence of renin-angiotensin-aldosterone activation. When the lesion affects both renal arteries or a single functioning kidney and is accompanied by renal failure (plasma creatinine concentration above 1.5 mg/dl), it is called ischemic nephropathy.

Atherosclerotic renal artery stenosis (RAS) may result in new onset of or worsening blood pressure management, deterioration of renal function and loss of renal mass, recurrent pulmonary edema, or unstable angina pectoris. Renovascular hypertension is the most common treatable cause of hypertension. Atherosclerosis accounts for at least two-thirds of all renovascular lesions.

### Prevalence

Renovascular hypertension accounts for the majority of patients with secondary hypertension and it is approximately 3% of hypertension within the general population. It should be suspected in patients with severe hypertension, particularly at the extremes of age. The mean age of patients with renovascular hypertension is over 50 years: two-thirds are male. Those presenting with ischemic nephropathy tend to be older. The probability of finding clinically significant renal artery disease correlates with the patient's age, the severity of hypertension, and the presence and severity of renal insufficiency. Atherosclerotic RAS is frequent in men with smoking history, elevated cholesterol levels, and diabetes. The prevalence on the basis of angiograms or autopsies is 35–45% in patients with atherosclerotic disease. The frequency of RAS in patients with abdominal aortic aneurysm, aortoiliac occlusive disease, and peripheral vascular disease is 38%, 33%, and 39%, respectively, on angiograms. The RAS greater than 50% occlusion is 15%. The prevalence of bilateral renal disease is 44% and approximately 59% in patients with one atrophic kidney and normal appearing contralateral kidney.<sup>1,2</sup>

### Natural history

Progressive renovascular disease (RVD) presents in patients with deteriorating blood pressure control, rising levels of creatinine, or episodes of flash pulmonary edema. These features indicate an extension of renovascular disease to both kidneys and/or dependence on a solitary functioning kidney. The lesion progression and accompanying clinical deterioration is common in patients with high-grade (greater than 75% diameter reducing) atherosclerotic RVD. Clinical deterioration will frequently present as progression to total renal artery occlusion, at which point some irreversible loss of function renal parenchyma has likely occurred. The silent progression of well documented in natural history studies. The cardio-renal artery stenosis and deterioration of renal function is vascular mortality rate in patients with RVH is worse than in those with essential hypertension.<sup>3-7</sup>

Zierler and coworkers have prospectively studied the progression of atherosclerotic RAS by sequential duplex ultrasonography. The cumulative incidence of progression of lesions with less than 60% reduction in lumen diameter progressing to more than 60% reduction in lumen diameter was 30% at 1 year, 44% at 2 years, and 48% at 3 years. Progression to total occlusion occurred only in arteries with a baseline reduction in lumen diameter of more than 60%. The cumulative incidence of progression to total occlusion in patients with baseline stenosis of 60% or greater was 4% at 1 year, 4% at 2 years, and 7% at 3 years.<sup>3</sup> Blood pressure control and serum creatinine were not predictors of progression. In patients with renal insufficiency the incidence of unsuspected RAS was 24%.

### Pathophysiology

The chief pathophysiologic mechanism underlying RVH involves activation of both limbs of the renin-angiotensinaldosterone system. The result is profound angiotensin-mediated vasoconstriction and aldosterone-induced sodium and water retention. In unilateral renal artery disease, sodium and water handling via pressure diuresis of the contralateral kidney may be sufficient to prevent a volume component to the hypertension.

Patients with bilateral RAS or those with a solitary kidney and a stenotic renal artery (functional bilateral RAS), manifest volume-dependent hypertension. These patients lack a normal kidney for naturesis, and the subsequent volume overload suppresses the renin-angiotensin system. This results in a volume overload state, which can lead to sustained hypertension and decompensated congestive heart failure. It has been reported that approximately one-quarter of patients with atherosclerotic renal artery disease will suffer pulmonary edema.

### Pathology

Renal artery occlusive disease is most commonly caused by atherosclerosis, followed by fibrodysplastic disease, and is rarely due to developmental lesions (Table 14.1).

Atherosclerotic renal artery stenoses (ARAS) are classified by location as either ostial or proximal lesions. Ostial renal artery stenoses are actually aortic wall plaque that encroaches upon the renal artery ostium. Proximal renal artery stenoses involve the main renal artery at least 1 cm beyond the ostium. In 80% of patients, these lesions represent a spillover type of lesion associated with aortic atherosclerosis. Non-ostial lesions comprise only 15–20% of all ARAS, with less than 5% involving the second or distal third of the renal artery. ARAS may be bilateral in approximately 50% of cases.

Ischemic nephropathy may be defined as a reduction in glomerular filtration rate (GFR) in patients with hemodynamically significant renovascular occlusive

**Table 14.1** *Causes of renovascular hypertension*

1. Atheromatous disease (70–80%)
2. Fibromuscular dysplasia (20–25%)
3. Dissecting aortic aneurysm
4. Renal artery aneurysm
5. Renal artery thrombosis Or embolism
6. Neurofibromatosis
7. Post-radiation fibrosis
8. Takayasu's arteritis
9. Dissection
10. Vasculitis

disease supplying the total functioning renal parenchyma. The term ischemic nephropathy is misleading and a better term is chronic azotemic renovascular disease. Within seconds of a reduction in renal perfusion pressure, there is a reduction in renal size due to reabsorption of fluid from the tubules and interstitial spaces, which is reversible. Pathologic changes in azotemic renovascular disease evolve from early changes of glomerular and tubular collapse, which are largely reversible, to later structural changes of interstitial fibrosis, cortical scarring, loss of nephrons, and progressive destruction of renal architecture with a loss of renal mass, which are irreversible (Figure 14.1).<sup>8</sup>

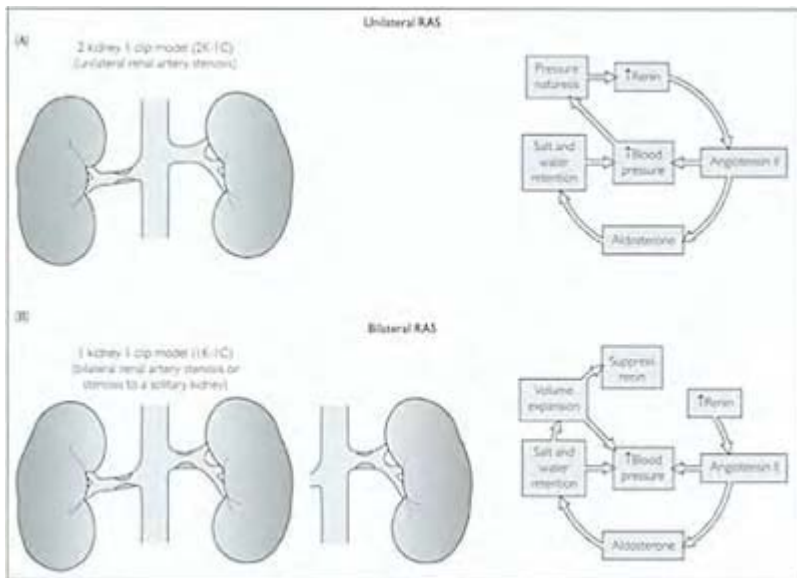
Fibrodysplastic disease is the second most common cause of renovascular hypertension. Medial fibrodysplasia is the most common type and is responsible for 85% of all types. It produces a string of beads classic angiographic picture and is more common in females in the 25–45 years age group and more frequent on the right side. Perimedial dysplasia is the next common lesion, causing about 10% of fibrodysplasia, and is seen in young women. Intimal fibroplasia accounts for 5% of all fibrodysplasia and produces long, irregular, tubular stenoses on angiogram.

cause of renovascular hypertension in children. They are Developmental renal artery stenoses are more common associated with developmental aortic-narrowing lesions, aortic coarctations, hypoplasia, and neurofibromatosis.

### Clinical presentation

Atherosclerotic RAS is the most common cause of secondary hypertension in the general hypertensive population. RAS in the young is usually due to fibromuscular dysplasia, and atherosclerosis occurs more often in older patients. Atherosclerotic RAS is incidental or it can present as uncontrolled hypertension, azotemia (ischemic nephropathy), and ‘flash’ or recurrent pulmonary edema. Hypertension in patients younger than 30 or older than 55 years of age should be evaluated for RAS. Malignant, accelerated hypertension or resistant hypertension, despite multidrug regimen, is associated with RAS. Patients with evidence of atherosclerotic disease—coronary, cerebral, or peripheral arterial disease—show increased likelihood of underlying RAS. The presence of a bruit is more frequently heard in the epigastrium and less often in the flank, and increases the likelihood of RAS. Bruit is present in 57% in fibromuscular dysplasia, 41% in atherosclerotic RAS, and in 7% in essential hypertension in renal arteries. Flash pulmonary edema, usually at night, without signs of severely impaired left ventricular function, is present in 41% of patients with bilateral ARAS and in 12% of patients with unilateral ARAS<sup>2</sup> (Table 14.2)

The RAS should be suspected in an elderly patient with azotemia that cannot be explained. The deterioration of



**Figure 14.1** (A) Mechanism of renovascular hypertension and hypertension in RAS (Goldblatt model)—unilateral RAS. (B)



## Mechanism of renovascular hypertension and hypertension in RAS (Goldblatt model)—bilateral RAS.

**Table 14.2** *Clinical clues to diagnosis of  
renovascular hypertension*

### 1. Hypertension

- a. Late onset (age >50 years) or early onset (before 30 years)
- b. Abrupt onset of moderate or severe hypertension
- c. Exacerbation of previously well-controlled hypertension
- d. Malignant or refractory to pharmacologic treatment
- e. Microvascular end-organ disease (grade III or IV retinopathy)
- f. Hypertension not improved on dialysis

### 2. Renal

- a. Unexplained (azotemia) (progressive renal failure) worsening of renal function with or without hypertension, with normal urinary sedimentation rate
- b. Worsening of renal function with the use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin II receptor blockers (ARBs)
- c. Unequal renal size or bilaterally small kidneys
- d. With D allele in the ACE polymorphism

### 3. Others

- a. Systolic/diastolic abdominal bruit (epigastrium/flank)
- b. Generalized atherosclerosis or cholesterol embolization, especially in smokers
- c. Recurrent unexplained episodes of heart failure—‘flash’ pulmonary edema in the setting of good ejection fraction

renal excretory function after the introduction of angiotensin-converting enzyme inhibitor (ACEI) or angiotensin II receptor blocker (ARE) therapy is an important clinical clue to the presence of significant bilateral RAS. RAS should be considered in a patient with a discrepancy in kidney size. Proteinuria <1 g in 24 hours is a discriminatory clinical sign, unless malignant hypertension or association with renal cholesterol crystal embolization are present.

## Diagnosis

Early identification and treatment of patients with significant RAS is important in order to decrease associated morbidity and mortality. Patients may present with hypertension, azotemia, and unexplained episodes of congestive heart failure or ‘flash’ pulmonary edema. The finding of hypertension in the face of systemic atherosclerosis, the discrepancy in renal size, or the hypertension and unexplained azotemia should prompt the clinician to search for RAS. The clinical clues presented in Table 14.2 should make the physician suspect underlying renal artery occlusive disease and the patient should be evaluated for the underlying cause.

### Noninvasive evaluation of RAS

Given the low prevalence of RVH, investigation should be based on the clinical history. Duplex ultrasonography, magnetic resonance angiography (MRA), and computed tomography (CT) angiography must be viewed as the primary screening tests for the diagnosis of RAS (see Table 14.3). When positive, these tests can reliably confirm the diagnosis of RAS.<sup>2,9</sup>

#### *Spiral CT scan with angiography*

Spiral CT scans using small amounts of intravenous (IV) contrast offer the diagnostic accuracy of arteriography and the lower risk of renal injury with IV digital subtraction angiography. Sensitivity and specificity of the spiral CT scan for detecting RAS are approximately 98% and 94%, respectively. CT angiography requires an IV contrast load, thereby making this a less useful tool in patients with preexisting azotemia.

#### *Magnetic resonance angiography*

MRA is becoming the preferred imaging test for diagnosing atherosclerotic renovascular hypertension especially in patients with mild renal insufficiency (Figure 14.2). Renal artery stenosis grading is done evaluating the 3-D gadolinium-enhanced and phase-contrast MRA. If the RA is stenotic in both gadolinium MRA and on 3-D phase contrast, MRA, but more severely stenotic on the 3-D phase contrast with dephasing, this should be considered hemodynamically significant severe stenosis. The sensitivity and specificity ranges from 73 to 100% and from 76 to 100%, respectively (Table 14.3).

#### *Duplex scanning*

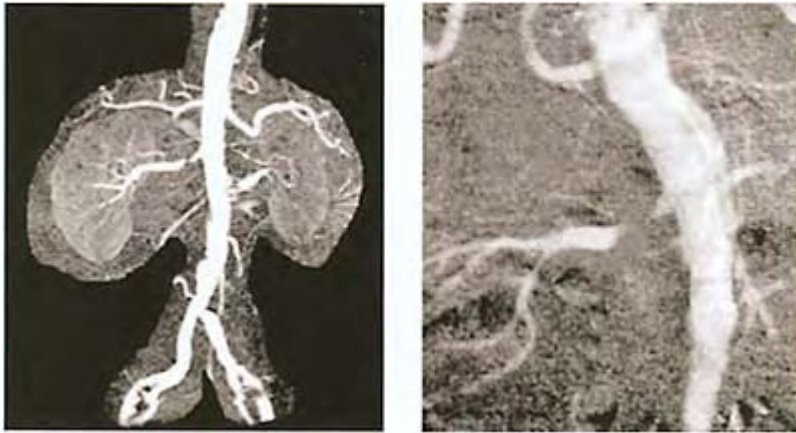
Renal duplex sonography is the preliminary study of choice for both renovascular hypertension and ischemic nephropathy. Duplex scanning can be done in a noninvasive vascular laboratory with 2.5–3.0 MHz low-frequency ultrasound transducers. A localized blood flow disturbance with a high-velocity jet indicates the presence of high-grade stenosis. Normal renal arteries typically show peak systolic velocities (PSVs) of less than 180 cm/s. The ratio of PSVs in the renal artery and aorta (RAR) is used as an index of severity of a renal artery stenosis (Table 14.4). Indirect criteria of RAS are rise time >0.07s, difference in resistive index >0.15 between kidneys or evaluated segmental arteries, loss of early systolic peak reflective wave complex.

Duplex ultrasonography is an excellent screening test because it provides anatomic information on the renal arteries, kidney size, and it is less expensive. Renal duplex has proven an accurate method to identify hemodynamically significant stenosis.

**Table 14.3** *Magnetic resonance angiography (MRA) grading of renal artery stenosis (RAS)*

| RAS grading   | MRA images                               |
|---------------|--|
| Normal        | Renal artery is normal in both studies   |
| Mild stenosis | RAS in one study but normal in the other |

|                   |   |
|-------------------|---|
| Moderate stenosis | RAS in both studies   |
| Severe stenosis   | Severe RAS on the 3-D gadolinium-enhanced MRA and occlusion on the phase-contrast MRA |
| Occluded          | Occlusion in both studies   |



**Figure 14.2** Algorithm for renal artery stenosis.

**Table 14.4** *Duplex criteria for renal artery disease*

| Renal artery status | Renal artery peak systolic velocity (PSV) | Renal/aortic ratio (RAR) |
|---------------------|---|--------------------------|
| Normal              | <180 cm/s                                 | <3.5                     |
| <60% stenosis       | 2:180 cm/s                                | <3.5                     |
| ≥60% stenosis       | ≥180 cm/s                                 | ≥3.5                     |
| Occlusion           | No signal                                 | No signal                |

cally significant renal artery occlusive disease with 93% sensitivity, 98% specificity, and 96% overall accuracy. Negative renal duplex effectively excludes ischemic nephropathy, since the primary consideration is global renal ischemia based on main renal artery disease. A kidney length of more than 7 or 8 cm has been advocated as a parameter favoring revascularization in patients with renal artery stenosis. Resistive indexes may be predictive of outcomes and should be obtained

The drawback is that it is not reproducible in all medical centers. The effects of respiratory motion and overlying bowel gas can also limit the success of renal duplex scanning. Renal arteries are especially difficult to examine because of their small size, deep location, and variable anatomy. Only 40% of the accessory renal vessels are currently identified with renal duplex.

### Functional tests

Although it may be desirable to establish the functional significance of RAS before revascularization, lack of sensitivity or specificity in many of the noninvasive tests has led most centers to intervene based on symptoms and the finding of an appropriate anatomic lesion. The tests used provide the physiologic functioning of the kidney and renin-angiotensin-aldosterone axis and are renal vein renin assays, captopril-enhanced renography and scintigraphy, and color Doppler ultrasonography (Table 14.5). Intravenous pyelogram, plasma renin activity, renal vein renin sampling are not used as diagnostic tests in current algorithms for diagnosis of RAS (Figure 14.3).<sup>2,9</sup>

Renal vein renin assays should demonstrate a ratio of renin activity exceeding 1.5:1.0 between involved and uninvolved sides before presumptive diagnosis of renovascular hypertension is established. The simplest test to evaluate the functional significance of a renal artery stenosis is determination of plasma renin activity (PRA). Unfortunately, neither renal vein renin assays nor split renal function studies are reliable when severe bilateral disease or disease to a solitary kidney is present.

**Table 14.5** *Screening tests for renal artery stenosis*

| Screening tests                            | Sensitivity | Specificity |
|--|-------------|-------------|
| RDS  | 90%         | 94%         |
| MRI/MRA                                    | 98%         | 91%         |
| Spiral CT                                  | 90%         | 97%         |
| <i>Functional studies</i>                  |             |             |
| Intravenous urography                      | 59%         | 89%         |
| RVRA                                       | 74%         | 90%         |
| Plasmin renin                              | 27%         | 95%         |
| Post-captopril renin levels (>5.7 ng/ml/h) | 96%         | 55%         |
| Captopril renography                       | 92%         | 95%         |

CT, computed tomography; MRI, magnetic resonance imaging; MRA, magnetic resonance angiography; RDS, renal duplex sonography; RVRA, renal vein renin assays

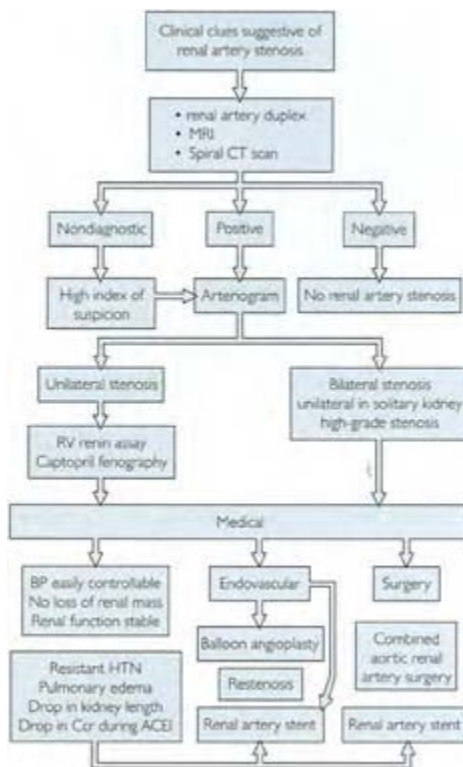
### *Captopril-enhanced renography and scintigraphy*

Renography with technetium-99m mercaptoacetyltriglycine (MAG 3) obtained before and after the administration of a single dose of captopril has been widely used to detect a functionally significant renal artery stenosis. Captopril-enhanced renography and scintigraphy is preceded by 50 mg of captopril given 1 hour before the procedure. A marked decline in GFR after the administration of an ACEI is presumptive evidence of the functional importance of the main renal artery stenosis. Captopril renography has sensitivity in identifying the renovascular disease of approximately 90% and specificity of 93% of cases. Multiple limitations are present in bilateral ARAS and in patients with advanced atherosclerosis and renal failure (serum creatinine  $\geq 2.5$  mg/dl); the patient should not take antihypertensive medications at least in the preceding 72 hours.

*Color Doppler ultrasonography*

A resistive index  $(1 - (\text{end-diastolic velocity} : \text{maximal systolic velocity}) \times 100) \geq 80$  before revascularization identifies patients with ARAS in whom revascularization will not improve renal function, blood pressure, or kidney survival.<sup>10</sup>

In patients with elevated creatinine levels, renal biopsy can be useful to detect the presence of important cholesterol crystal renal embolization or severe histopathologic



**Figure 14.3** Alfg gorithm for renal artery stenosis. ACEI, angiotensinonco nverting enzyme inhibitor; BP, blood pressure; Ccr, cre eatinine; CT, computed tomography; HTN, hypertension; MRI, ma agnetic resonance imaging; RV, renal vein.

re nal damage (high degree of glomerulosclerosis and/or bulointerstitial sclerosis), which is an important determ inant and predictor of renal function outcome.

## Angiography

Arteriography is the gold standard for the diagnosis of RAS. If the clinical suspicion for HAS is high, even with negative noninvasive studies, the patient should undergo arteriography, especially if intervention will be offered in the face of positive results.

The arteriogram examination should begin with flush aortogram to determine the number and location of the renal arteries; this may avoid the risk of unnecessary selective catheterization in patients with widely patent arteries. In addition, the presence of an abdominal aortic aneurysm or marked aortic atherosclerosis may be delineated, and should be documented. Multiside hole catheter is used and contrast is injected at a rate of 25 ml/s for a total of 40 ml and 1000 psi maximum pressure. Anterioposterior, 20° (left anterior oblique) (LAO) and 40° LAO projection films are taken to view the renal artery origins. Craniocaudal angulation is occasionally necessary, particularly for the evaluation of branch renal artery lesions or stenoses occurring in transplant renal arteries. An iso-osmolar, nonionic contrast agent is recommended in patients who have impaired renal function or who are at high risk of developing contrast-induced nephrotoxicity. In high-risk patients with elevated creatinine levels, gadolinium or carbon dioxide are used.

## Indications for intervention

Hemodynamic significance implies a stenosis causing  $\geq 50\%$  diameter reduction relative to the normal reference vessel diameter and a significant pressure gradient across the lesion. A stenosis is considered significant if there is a greater than 15% peak systolic blood pressure gradient present (change in peak systolic pressure  $\times 100$ /aortic peak systolic blood pressure) or 10 mmHg difference in mean arterial pressure or 20 mmHG peak systolic pressure. The criteria for duplex ultrasound (US) evaluation of the renal arteries uses a vessel categorization of  $>60\%$  diameter stenosis.

Poorly controlled hypertension is the most common indication for revascularization. Trends in both surgical and endovascular intervention in renal artery stenosis have shifted toward patients with progressive renal dysfunction in order to improve or prevent the relentless decline in renal function over the past decade.

The value of prophylactic renal revascularization in patients without clinical manifestations of disease (i.e. hypertension, renal insufficiency, cardiac disturbance) is unproven.<sup>11</sup> Based on the natural history of the disease process, it would be appropriate to intervene in those patients with ostial or main vessel stenoses of  $>75\%$ , regardless of hypertension. This remains a source of ongoing debate. The intervention is less useful in patients with severe renal dysfunction (i.e. GFR  $<30$  mL/min, creatinine  $>250$  mmol/l), reduced kidney size ( $<7$  cm), impaired renal function, extensive nephrosclerosis of the target kidney, or extensive vascular disease. Renal biopsy before intervention may help to exclude the patients who have severe parenchymal damage. Patients in whom there is a history of severe idiosyncratic contrast material reaction should be excluded for renal artery stent.

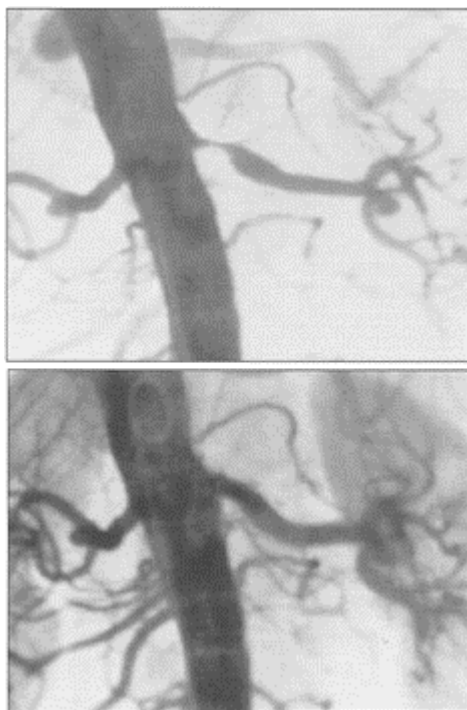
The clinical criteria for revascularization in the presence of a significant RAS are:

1. Hypertension: accelerated hypertension (sudden worsening of previously controlled hypertension); refractory hypertension (hypertension resistant to treatment with at least 3 medications of different classes, including a diuretic); malignant hypertension (hypertension with coexistent evidence of end-organ damage, including left ventricular hypertrophy, congestive heart failure, visual or neurologic disturbance, and/or advanced (grade IV) retinopathy); hypertension with a unilateral small kidney; and hypertension with intolerance to medication.
2. Renal salvage: sudden unexplained worsening of renal function; impairment of renal function secondary to antihypertensive treatment, particularly with an ACEI or an ARE; renal dysfunction not attributable to another cause.
3. Cardiac disturbance syndromes: recurrent 'flash' pulmonary edema out of proportion to any impairment of left ventricular function; unstable angina in the setting of significant RAS.<sup>11</sup>

### **Selection of therapy**

The silent progression of renal artery stenosis and deterioration of renal function is well documented in natural history studies and the medical therapy outcomes have been disappointing. The surgical revascularization is effective and durable but is associated with a significant risk of complications. Recent technical advances have resulted in improved outcomes after angioplasty and renal artery stenting (Figure 14.4).

Most atherosclerotic renovascular lesions are relatively focal in nature and are therefore amenable to angioplasty or stent placement. For non-ostial lesions, angioplasty is sufficient except where there is an indication to stent: namely, excess elastic recoil, inadequate dilatation, or partial dissection. Intervention for ostial lesions (within 1 cm of the origin) should be by percutaneous transluminal renal angioplasty (PTRA) plus stenting or a surgical revascularization procedure. Post-angioplasty restenosis was also a common indication for stents. Unusually long lesions are often treated surgically. Completely occluded renal arteries may be successfully recanalized percutaneously in some cases; however, bypass surgery is usually recommended if a patent distal target artery can be identified and the kidney size is >8.0 cm. In patients about to undergo vascular surgery for other problems (e.g. treatment of abdominal aortic aneurysm, renovascular disease) it may be best corrected simultaneously. However, the morbidity and mortality of aortic surgery are thereby increased. Some patients with very difficult to control hypertension may be better treated by percutaneous renal vascularization prior to or following surgery. Although the presence of risk factors usually weighs in favor of percutaneous treatment,



**Figure 14.4** Renal artery angioplasty.

some risks may favor surgery. At some institutions, solitary kidneys are revascularized surgically to reduce the risk of kidney loss. Bush et al.<sup>12</sup> report good results with renal artery stenting in solitary kidneys. Surgery is the preferred modality in patients with renal artery occlusion that cannot be traversed, an aorta that is known to have excessively friable plaque, or an anatomically inaccessible renal artery. Ischemic nephropathy is best treated before the development of advanced renal failure, either by stenting or surgical revascularization. The best candidates for revascularization are those with baseline serum creatinine less than 2.0 mg/dl, bilateral renal artery stenosis, normal renal resistive indices, no proteinuria, and one or more manifestations of endorgan injury.

### **Medical therapy**

The fundamental objectives of RVH treatment are to preserve or maintain renal function in addition to controlling blood pressure. Aggressive medical therapy for risk reduction and blood pressure control must be undertaken irrespective of revascularization. The blood pressure control in renovascular hypertension can be achieved in many cases with medical therapy. Medical therapy usually requires a combination of antihypertensive drugs ( $\beta$ -blockers, ACEIs, diuretics, ARBs) to control the blood pressure in 90% of cases but does not prevent the progression of the vascular lesions. Renal function should be



monitored regularly and if it deteriorates, intervention should be offered early rather than late where irreversible changes in renal parenchyma.

## Endovascular therapy

### *Introduction*

Gruntzig first described percutaneous renal artery angioplasty in 1978 and it was later described by Tegtmeier and Sos. The recent development of specialized diagnostic catheters, wires, balloon catheters, and flexible stents has renewed interest in percutaneous management of RVD (Table 14.6). In some centers, primary stenting of renal artery stenoses is the norm rather than the exception.

### *Approaches*

RAS is usually performed by femoral approach and sometimes using a radial<sup>13</sup> or brachial arterial approach. The route of access is selected on the basis of anatomic and pathologic features (atherosclerotic disease, tortuosity, and abnormalities of aorta and iliac vessels, aneurysm with thrombus) of aorta and renal artery origins that are assessed by MRA, duplex scan, or diagnostic angiogram. The brachial or radial approach is selected especially if the infrarenal aorta is occluded, infrarenal aorta with friable plaque and the renal artery origin is cephalad or with acute aorto-renal angles.<sup>13</sup> Current technology, with flexible stents which adhere well to their delivery systems, enables traversal of even the most acute bends at the renal artery origin. The major limitations of the brachial approach are the smaller size and longer sheaths and catheters that are difficult to manipulate, and a higher percentage of access-related complications.

### *Nonselective and selective angiography*

The femoral approach is favored when the renal arteries are oriented horizontally or caudally with respect to aorta. Vascular access is typically obtained using a 6 or 7F sheath,

**Table 14.6** *Catheters and stents used in renal artery stenosis*

1. Catheters in nonselective aorto-renal angiography:
  - a. Conventional pigtail
  - b. Tennis racket
  - c. Omni flush
  - d. Straight flush with multiple side holes
2. Diagnostic catheters used for selective renal angiography:
  - a. Renal double curve
  - b. Cobra
  - c. Judkins right

- d. Left internal mammary
  - e. Sos omni
  - f. Berenstein
  - g. Simmons-1
  - h. Simmions-2
3. Guiding catheters used in renal stenting:
- Hockey stick
  - Renal double curve
  - Left internal mammary
  - Renal double curve-1
  - e. Multipurpose
4. Renal stents:
- a. Cordis (Miami, Florida):
    - i. Palmaz '04 series'
    - ii. Palamaz long medium
    - iii. Corinthian IQ
  - b. Intratherapeutics (ITI; St Paul, Minnesota):
    - i. Single sturt
    - ii. Double sturt
  - c. Medtroincs/AVE (Santa Rosa, California):
    - i. Bridge Stent
  - d. Guidant (Santa Clara, California):
    - i. Megalink
    - ii. Herculink
  - e. Boston Scientific/Medinol (Watertown, Massachusetts) NIR Peripheral

advanced under direct fluoroscopic control over a 0.035 inch guide wire. A number of catheters, in 4, 5, or 6F diameters are available for nonselective angiography. The catheter is placed at the top of the first lumbar vertebral body. A conventional pigtail catheter leads to retrograde flow of contrast, spilling over to the SMA or celiac artery. Tennis racket and omni flush catheters offer the advantage of more lateral and less retrograde/cephalad contrast flow, which results in reduced filling of the SMA. Typically, 20–30 ml of dye is injected at a rate of 10 and 15 mls. A larger aorta may require more volume and/or a higher injection rate. Gadolinium or CO<sub>2</sub> are used in order to minimize contrast exposure in patients with elevated creatinine levels. A mainstream aortic injection with at least two oblique views (20° and 40° LAO) should be obtained. The right renal artery typically arises from the mid-coronal plane or anterior to this; the left is less constant and can arise from anterior or posterior to the mid-coronal plane. Nonselective angiography provides valuable information about the orientation and configuration of aorta and the location and orientation of the renal ostia, and facilitates selective renal artery cannulation with minimal manipulation. It also identifies the dual renal supply or accessory renal arteries. The disadvantage is use of additional contrast. Selective cannulation of the renal artery was performed using a soft-tipped, 4, 5, or 6F diagnostic catheter.

*Renal artery angioplasty*

After selective cannulation of the renal artery, 5000 U of heparin and nitroglycerin 150 µg are given through the catheter. A guide wire is then passed across the lesion and the diagnostic catheter is then exchanged for the balloon angioplasty catheter. Various shapes are available and should be selected based on the size and configuration of the aorta and orientation of the renal arteries. The balloon is removed after dilation of the lesion. Diagnostic angiography should not only include the appropriate views of the renal artery and the lesion but should also include a careful assessment of the baseline nephrogram. A guide wire, (0.035 inch) which is atraumatic, soft tipped and steerable is then carefully inserted into the renal artery through the diagnostic catheter: Wholey wire (Mallinkrodt, St Louis, Missouri); the Storque wire (Cordis Corporation, Miami, Florida); and the Magic Torque wire (Boston Scientific Corporation, Watertown, Massachusetts). If the vessel is critically narrowed or there is significant irregularity of the plaque at the ostium, precluding the passage of a 0.035 inch wire, a 0.014 inch or 0.018 inch guide wire system can be used. In general, hydrophilic guide wires should be avoided during renal intervention, due to the risk of dissection and distal perforation. Once the lesion has been traversed, the angioplasty balloon catheter is advanced across the lesion. The guiding catheters allow the injection of contrast and vasodilators as required. The guiding catheters simplify diagnostic angiography during the intervention, provide excellent backup for insertion of the balloon catheters, facilitate the use of dual guide wires to protect side branches, and afford the opportunity to measure simultaneous translesional pressure to assess the hemodynamic effect of balloon dilatations, all through a single arterial access site. The balloon diameter should match that of the normal renal artery, usually 6 mm in females and 7 mm in males. The most common cause of failure of renal artery angioplasty is immediate elastic recoil; the second most common cause is a significant dissection.

*Renal artery stealing*

Current indications for stent placement are poor immediate results during percutaneous transluminal angioplasty (PTA) as well as restenosis after PTA (Table 14.7). The frequent association of dense calcification and common ostial location of these lesions resulted in early recoil related lumen loss amplifying the restenosis process after angioplasty. Stents are also used to treat angioplasty complications (artery dissection and intimal flaps) and thus have markedly reduced the incidence of emergency surgery for these complications. 'Primary' stent placement is becoming increasingly popular in cases of RAS in which PTA alone is unlikely to be successful (ostial lesions). The concept of providing scaffolding via an endovascular prosthesis or stent renewed interest in transcatheter intervention for renal artery stenosis in the 1990s. The first-generation stents were slotted tube designs, lending to their inherent rigidity and adversely affecting the deployment characteristics. A transbrachial approach by Dorros and several transfemoral techniques were described to place renal artery stents. Now more flexible stents and stent delivery systems, specifically designed for renal stent placement, are available (Figure 14.5). The first renal artery stent procedure in the United States was performed in 1987 using a coronary version of the Palmaz stent (Cordis, Division of Johnson & Johnson, Warren, New Jersey) as part of the United States Multicenter Trial.

The ideal renal stent should have the following characteristics: good radiopacity, no shortening; ability to negotiate acute angles; and good radial strength. Hoop strength

**Table 14.7** *Indications for renal artery stenting of a hemodynamically significant renal artery Stenosis*

1. Immediate failure of balloon angioplasty (suboptimal percutaneous transluminal renal angioplasty (pTRA)/acute complication):
  - a. Large dissection flap
  - b. Significant residual pressure gradient
  - c. Residual stenosis >30%
  - d. Elastic recoil from an ostial lesion
2. Stenosis of the ostium of a renal artery that has a normal diameter of 5 mm or greater
3. Restenosis of a lesion that was successfully treated with balloon angioplasty in the past

must be adequate throughout the length of the stent, including the edge that protrudes minimally into the aorta, in order to resist the strong compressive forces of heavily calcified ostial plaques. In cases of ostial lesions, the stent should be placed to protrude 1–2 mm into the aortic lumen to prevent restenosis due to recoil of the aortic plaque.

Technical success, as defined by minimal residual luminal encroachment and successful stent deployment without immediate periprocedural major complication, can be achieved in most patients (95–100%).<sup>2</sup> Pressure gradients can be measured before and after angioplasty/ stenting to determine the efficacy of the procedure. The gradient is measured distal to the lesion and, in aorta, close



**Figure 14.5** Atherosclerotic bilateral renal artery stenting.

to the renal ostium. Technical failure is defined as the inability to deploy the stent, residual stenosis >30%, and/or persistent gradient.<sup>14</sup>

### *Complications*

Complications of arteriography predominantly fall into three groups: access-related complications, contrast-induced nephropathy, and atheroembolic disease. The access-related complications are pseudoaneurysms, arteriovenous fistulae, hematomas, retroperitoneal bleed, thrombosis, or infection<sup>2</sup> (Table 14.8) In contrast-induced nephropathy, the serum creatinine begins to rise 24–48 hours following contrast administration, peaks within 3–5 days, and then returns to baseline levels within 7–10 days. In patients with severe nephrotoxicity, the serum creatinine may continue to rise for 5–10 days or until dialysis is required. The elevation of creatinine 72 hours following the procedure is most likely related to atheroembolization. The incidence of contrast-induced nephropathy in non-high-risk patients has been quoted at 0–7%, with an average of 3%. High-risk patient groups include diabetes mellitus, multiple myeloma, and pre-existing impaired renal function. Other major complications are acute renal failure, cholesterol embolization, and ischemic bowel.

### **Outcomes of endovascular therapy**

Angioplasty and stenting of renal artery stenoses have been shown to be technically feasible and successful; predicting which patients will have improvement in blood pressure or renal function post-intervention has been difficult. The discrepancy between the angiographic success and the clinical/physiologic success is not yet clearly understood. The procedural success is not dependent upon simply getting the artery open but also depends on atheroembolization during the procedure and the amount of contrast used (Table 14.9).

**Table 14.8** *Renal stent complications*

|                                      |       |
|--------------------------------------|-------|
| Restenosis                           | 17.0% |
| Mortality                            | 2.1%  |
| Complications:                       | 16.4% |
| Puncture site complications          | 5.9%  |
| Renal failure                        | 5.0%  |
| Kidney or renal artery complications | 3.5%  |
| Miscellaneous                        | 1.9%  |

### *Technical success*

Technical success is usually defined as a residual stenosis of  $\leq 30\%$  with diminished pressure gradient  $< 5\text{mmHg}$  across the lesion after renal artery stenting and in atherosclerotic renal artery stenosis the rate of technical success reported in the literature is 98–100%. The most common cause of failure was immediate elastic recoil, with a significant dissection as the second most common cause.

*Clinical success*

Improvement in blood pressure after renal artery angioplasty/stenting may be seen as early as 4–6 hours after the procedure and is more commonly observed after 48 hours. The maximal antihypertensive effect may not be seen for several weeks. Clinical success refers to complete or substantial relief of presenting symptom, be it hypertension, azotemia, or both. Hypertension was cured (normotensive/off medication) in 9% and improved in 52%, with a cure or improvement in 61% of patients at the latest follow-up interval. In patients with renal failure, 25% showed long-term improvement of function, with stabilization in another 57%.

Despite technically successful renal artery reconstruction, on average serum creatinine does not change. Average values for the group are misleading. Nearly 50% of patients subjected to revascularization will have no meaningful change in kidney function on long-term follow-up (stabilized renal function); 25–30% of patients have improved renal function. But renal function deteriorates substantially during the period after revascularization in about 18–25% of patients. It is the presence of this group that prevents the inference of an overall group benefit and leaves the mean level of creatinine unchanged. Some of these patients lose kidney function due to atheroembolic complications.

*Medical therapy vs angioplasty*

There are three randomized prospective trials comparing medical management with angioplasty for blood pressure control in patients with ARAS (210 patients).<sup>15–19</sup> The largest randomized, prospective study was recently published by van Jaarsveld et al;<sup>15</sup> in this study 106 patients were treated either conservatively or by angioplasty. Interventional treatment had little advantage over drug therapy, but angioplasty resulted in a reduction of antihypertensive medication. There was a relatively high crossover rate of patients initially treated conservatively who later received angioplasty.<sup>15</sup> Balloon angioplasty was significantly more effective than medical therapy in

**Table 14.9** *Results of endovascular and surgical intervention for atherosclerotic renal artery stenosis*

|                                 | PTRA | Stent | Surgery | Surgery after failed PTRA |
|---------------------------------|------|-------|---------|---------------------------|
| No. of Patients                 | 1179 | 1045  | 525     | 28                        |
| Technical success               | 84%  | 98%   |         |                           |
| Patients with renal dysfunction | 177  | 436   |         |                           |
| Renal functional response:      |      |       |         |                           |
| Improved                        | 35%  | 25%   | 50%     | 47%                       |
| Unchanged                       | 53%  | 57%   | 39%     | 43%                       |
| Worsened                        | 12%  | 18%   | 11%     | 10%                       |
| HTN response:                   |      |       |         |                           |
| Cured                           | 12%  | 9%    | 18%     | 11%                       |
| Unchanged                       | 58%  | 52%   | 71%     | 78%                       |
| Worsened                        | 30%  | 39%   | 11%     | 11%                       |

|               |      |     |      |      |
|---------------|------|-----|------|------|
| Restenosis    | 22%  | 17% | 5.7% | N/A  |
| Complications | 13%  | 16% | 21%  | N/A  |
| Mortality     | 1.7% | N/A | 3.6% | 4.3% |

HTN, hypertension; PTR, percutaneous transluminal renal angioplasty.

lowering the blood pressure of hypertensive patients with atherosclerotic renal artery stenosis, and resulted in the use of less antihypertensive medication and perhaps fewer major cardiovascular and renovascular complications in other studies.<sup>15–17</sup> None of the trials showed a significant improvement in renal function with angioplasty, despite a higher arterial patency rate with balloon angioplasty. Although it also produced a higher patency rate, this technical success did not improve renal function.

### *Stenting in renovascular hypertension*

In proximal renal artery stenosis, most angioplasty reports have more than 80% technical success rate with a 68–90% clinical success rate and 5-year patency as high as 88%<sup>2,12,20–23</sup> A 20% reduction in pretreatment creatinine in patients with renovascular azotemia can be achieved in approximately half of patients after PTA of bilateral RAS or stenosis in the artery to a single kidney. Angioplasty of unilateral RAS in patients with two kidneys and azotemia provides no benefit in stabilization of renal dysfunction.

Angioplasty of ostial atherosclerotic stenoses has a low rate of technical success, due to the elastic nature of aortic wall plaque. The stent placement is technically successful in 94%, with complications in 9.1%, and with a restenosis rate in 16% at the end of 1 year.<sup>22</sup> The success of percutaneous intervention for atherosclerotic RAS depends on the operator selection of patients, technical skill, and the case mix. Bush et al reported renal artery stenting in 27 patients with a solitary functioning kidney, and demonstrated this treatment modality to be a relatively safe alternative to conventional surgery in this high-risk patient group. Most (74%) of the patients in this series had improved or stabilized renal function.<sup>12</sup> The largest series (1058 patients) on renal artery stenting was reported by Dorros et al, who showed that in patients with normal or only mildly impaired renal function, renal artery stenting was beneficial for blood pressure control and preservation of renal function.<sup>23</sup>

Restenosis after angioplasty occurred in 30% of the patients with angiographic follow-up and in 15–20% of patients with stents.<sup>2</sup> Restenosis of lesions treated with angioplasty is often managed effectively by repeat angioplasty or stenting with good secondary patency rates. Post-angioplasty restenosis was also a common indication for stents.

### *Stent vs angioplasty*

Most atherosclerotic lesions are now treated initially by angioplasty with balloon-expandable stent placement because most patients with ARAS have ostial or proximal disease. This procedural shift is based on observational studies suggesting that stenting may be superior technically and comparable clinically to balloon angioplasty. Whereas blood pressure control and improvement or stabilization of renal function may occur with PTA alone, the restenosis rate is high without the use of a stent.<sup>12,19–23</sup>

A randomized trial of treating ostial atherosclerotic renal artery stenosis showed that the changes in blood pressure and renal function were similar in the stenting and angioplasty groups at 6 months but that stenting resulted in a lower acute restenosis rate and higher long-term patency rate than did angioplasty alone (14% vs 48%).<sup>24</sup>

#### *Angioplasty vs surgery*

A trial comparing surgery and angioplasty has shown that surgical revascularization led to a higher patency rate than balloon angioplasty, but this technical success did not improve clinical outcomes. There was no difference in blood pressure control and renal function between these groups.<sup>25</sup>

#### *Stenting vs surgery*

There is no level 1 evidence of the superiority of surgical versus endovascular stenting of the renal artery. The stenting has vastly improved the unfavorable results of PTA alone for ostial lesions. Mode of intervention is selected according to individual patient age, clinical circumstance, and comorbidity. The majority of failures in renal artery surgical reconstructions are technical in nature and occur in the early postoperative period. Operative mortality, early graft failure, and eventual need for reoperation are around 5%.<sup>26</sup>

#### *Influencing factors/prognosis*

Prediction of the results of renal vascularization in a specific patient remains an elusive goal. There are no specific studies to assure a favorable outcome within the kidney. The results of angioplasty for fibromuscular dysplasia are 25–45% cure rate and for atherosclerotic stenosis the cure rate is around 10–15%.

Age beyond 65 years old, gradual loss of kidney function, widespread atherosclerotic disease of the aorta, and diabetes all predict less favorable outcome (Table 14.10). A study by Giroux et al also found that a shorter duration of hypertension, higher diastolic blood pressure, and fibro-muscular renovascular disease were predictive of a favorable clinical outcome after percutaneous revascularization. In addition, patients with less atheromatous aortic disease and a more severe angiographic stenosis were also more likely to have a favorable clinical response with a strong association in hypertensive patients and a weak association in renal insufficiency patients.

In patients with impaired renal function, patients with a lower baseline serum creatinine (1.5–3.0) and a higher

**Table 14.10** *Factors that influence the success of renal revascularization*

#### **Adverse prognostic factors**

##### *General*

Females

Age beyond 65 years

Diabetes



Smoking history Widespread atherosclerotic disease of the aorta

#### *Renal factors*

Small kidneys

Impaired renal function (creatinine >3.0 mg/dl)

Gradual loss of kidney function

Atherosclerotic renal artery ostial stenosis

Small vessel intrarenal disease on angiography

Nonlateralization of the renal scintigram

Resistive index at Doppler sonography

Rate of decline of renal function

#### **Atherosclerotic renal artery stenoses (ARAS) angioplasty**

Technical success:

Ostial 75%

Nonostial 84%

Patency rates for angioplasty:

Plouin 19% 1 year follow-up

Jensen 24% 1 year follow-up

Clinical success:

Ramsey 24%+43% (C+I) in collected series

Martin 50% after 5 years

Stents:

Patency

Primary at 1 year 93%

at 2 years 77%

Secondary at 1 year 98%

at 2 years 93%

#### **Medical vs angioplasty vs surgery**

Plouin (medical vs angioplasty—49)

Angioplasty: 26% no medications; 35% (2 or more medications)

Medical treatment: 0% no medications; 88% (2 or more medications)

Weibull (surgery vs angioplasty—58)

|                   | Surgery | Angioplasty      |
|-------------------|---------|------------------|
| Technical success |         |                  |
| Initial           | 97      | 83               |
| Primary patency   | 96      | 75 after 2 years |
| Secondary patency | 97      | 90 after 2 years |

No difference between blood pressure control and renal function between these groups

GFR had a better clinical response after renal artery stenting at follow-up. In patients with more advanced renal failure (serum creatinine concentration >4.0mg/d), significant underlying irreversible renal parenchymal disease invariably exists. Some authors observe that those patients with more recent loss of renal function, e.g. those with a rise of serum creatinine within a few months prior to revascularization, are more likely to recover function than those with slow, progressive loss of function. Parenchymal damage

may be the key to determine an indirenal disease—urinary protein excretion  $>1$  g/day, hypervidual patient's outcome, The indicators of parenchymal uricaemia, and a creatinine clearance  $<40$  ml/min—may identify a subgroup of patients who are less likely to benefit from renal revascularization.<sup>27</sup>

Small kidneys ( $<7$  cm) by radiographic or ultrasound imaging are less likely to recover function than larger kidneys. The lateralization of the renal scintigram prior to stent placement was a highly significant predictor of clinical success in patients treated for hypertension or renal function impairment. The presence of small vessel intrarenal disease on angiography had an adverse effect on blood pressure and renal function response (Figure 14.6). Renal artery end-diastolic velocity (EDV  $>90$ ) and renal artery resistance index (RI  $<75$ ) are good predictors of positive outcome after renal artery stenting, i.e. improvement in serum creatinine and control of blood pressure. Long-term hypertension may cause nephrosclerosis or glomerulosclerosis, and increase vascular resistance. Radermacher et al demonstrated that a renal artery RI  $>80$  has good predictive value in identifying patients who are unlikely to benefit from renal revascularization.<sup>10</sup> Higher EDV ( $>90$ ) and a lower RI ( $<75$ ) identify HAS patients who are without microvascular disease or increased resistance in the segmental arteries and are likely to benefit from renal stenting.<sup>28</sup>

### *Patency*

Females are more likely to develop restenosis than males. Smoking history was associated with a twofold risk of restenosis. Lesions with stents that were dilated to less than 6 mm are more likely to develop restenosis. Patients with a focal stenosis without plaque accumulation, as determined by intravascular US, did better than patients with an accumulation of atherosclerotic plaque at their stenosis.

## **Surgical revascularization**

Renovascular hypertension can be treated surgically using a variety of techniques. Reconstructive techniques include renal artery bypass, endarterectomy, and renal reimplanta



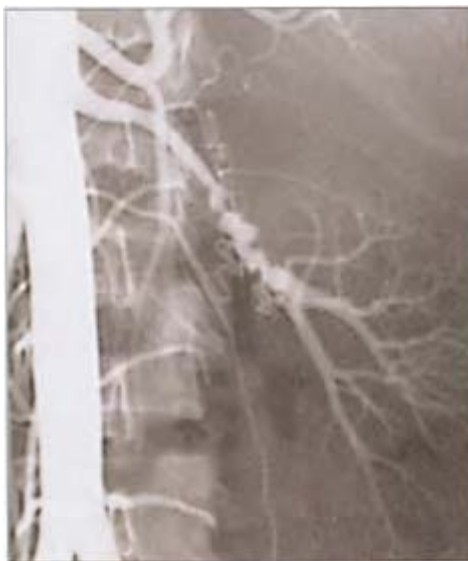
**Figure 14.6** Atherosclerotic small vessel disease in the kidney.

tion. In patients who have severe hypertension and nonreconstructable renal arteries or small dysfunctional kidneys, nephrectomy is an alternative. Surgery is the preferred modality in patients with renal artery occlusion that cannot be traversed, an aorta that is known to have excessively friable plaque, or an anatomically inaccessible renal artery.

If an infrarenal aortic graft is needed, then anatomic renal artery reconstruction either by means of transaortic endarterectomy, or with an aortorenal sidearm graft originating from the main aortic graft, is the preferred technique. In contemporary practice, combined aortic and renal artery grafting accounts for 50% of renal artery reconstructions. Extra-anatomic reconstruction is used in many patients when unilateral renal artery reconstruction is indicated, especially in patients with redo surgery, in high-risk patients, and hostile aortas. The durability of extra-anatomic reconstructions is equivalent to aortorenal bypass.<sup>26</sup>

### Other renal artery diseases

Patients with true renin-dependent (renovascular) hypertension are typically young or middle-aged women with renal fibromuscular dysplasia (FMD) (Figure 14.7). Initial therapy for renovascular hypertension associated with FMD is an ACEI; refractory hypertension responds readily to balloon angioplasty without stenting. Renal artery aneurysms (RAAs) can cause renovascular hypertension and can infrequently result in significant morbidity and



**Figure 14.7** Fibromuscular dysplasia of the left renal artery.

mortality due to rupture. The symptomatic RAAs can be treated with covered stents (Rundback type I RAA) or sometimes with coil embolization (type III RAA) and type II aneurysms are better treated by open surgery or even nephrectomy.<sup>29,30</sup> There are case reports reporting good results in patients with acute aortic dissection and renovascular hypertension utilizing endovascular therapy.<sup>31</sup> In Takayasu's arteritis in the absence of active disease or inflammation, angioplasty has been performed to relieve RVH as well as to prevent renal loss, with 80% technical success and overall clinical benefit in the range of 85%.<sup>32</sup> The etiologies of RVD in children are fibromuscular dysplasia, middle aortic syndrome, neurofibromatosis, Williams syndrome, arteritis, and surgical abdominal trauma. There are reports of good results after PTA.<sup>33</sup> Endovascular treatment of renal artery thrombosis caused by umbilical artery catheterization in association with aortic thrombosis has been reported with resolution of systemic hypertension and partial return of right renal function followed by rapid thrombus dissolution with thrombolysis.<sup>34</sup>

### Follow-up

The purpose of monitoring is to detect a change within a time frame that minimizes the chances of irreversible damage. Preprocedure assessment includes renal size, GFR, and blood pressure. The patients with 50–75% stenosis are regularly monitored and the patients with progressing lesions are treated with renal angioplasty/stenting. A decrease in renal size of >1 cm, a decrease in GFR of > 20%, or an increase in mean arterial blood pressure >10 mmHg should prompt further assessment in the form of a repeat renal

angiogram. After endovascular intervention, GFR and blood pressure are assessed during the first month and thereafter 6 monthly in conjunction with a renal US scan.

## Conclusion

The salient points are the following:

- Atherosclerotic renal artery stenosis is a progressive disease leading to hypertension, renal failure, and shortened survival.
- The role of renal duplex study is underutilized as a screening study.
- In aggressive medical therapy for risk reduction, blood pressure control must be undertaken irrespective of revascularization.
- Choice of therapy should be individualized.
- Surgical revascularization cures/improves hypertension and improves/stabilizes renal function in approximately 75% patients but is complicated by a mortality of 4–6%.
- PTRAs cures/improves hypertension and improves/ stabilizes renal function in two-thirds of the patients but has a high rate of restenosis.
- Renal stent revascularization procedural results have been demonstrated to be superior to balloon angioplasty, as assessed by hemodynamic trans-stenotic pressure gradient measurements, complication rates, and restenosis rates. The preferred technical modality of treatment is renal stenting.
- Even though there is trend for endovascular therapy for severe RAS (> 80%) in asymptomatic patients based on natural history studies, the value of prophylactic renal revascularization in patients without hypertension and renal insufficiency is not yet proven.
- Randomized trials comparing PTRAs to medication have shown minor improvement in hypertension control, reduction in the number of antihypertensive medications, and no effect on renal function.
- The treatment of choice for renal artery occlusive disease has shifted from open repair to percutaneous angioplasty and stenting in many institutions, as morbidity and mortality of renal artery stenting compared to surgery is lower.
- Better-designed randomized prospective trials with long-term follow-up are required to provide evidence for unanswered questions.

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## 15

# Laparoscopic surgery for renovascular disease

Sidney C Abreu and Inderbir S Gill

### Introduction

In recent years, minimally invasive percutaneous techniques performed by interventional radiologists have become increasingly popular for the treatment of surgically curable renovascular disease. Percutaneous transluminal balloon angioplasty and intravascular stenting are effective and safe alternatives for the management of renal arterial stenosis.<sup>1</sup> As such, with the exception of an occasionally complex renovascular lesion, the majority of the renal arterial stenoses are currently being treated by endovascular techniques.<sup>2</sup> However, for renal artery aneurysm or branch arterial disease, revascularization remains the procedure of choice to control hypertension and preserve kidney function. Open renal revascularization is a major and highly precise surgical procedure, requiring a large skin incision with its attendant postoperative morbidity.

Laparoscopic techniques have gained acceptance in urology for certain ablative surgical indications. However, laparoscopy has not been applied clinically for renovascular surgery, because of the high degree of technical precision and renal ischemia considerations involved therein. At the Cleveland Clinic animal laboratory, our team has investigated the feasibility of applying laparoscopic techniques for renal revascularization surgery. Although the results of these preliminary studies have been encouraging, they have not yet been applied in the clinical setting.

### Arterial bypass and aortorenal bypass

Laparoscopic arterial bypass surgery was initially explored in 1995 by Ahn and Clem,<sup>3</sup> who described aortofemoral bypass in an animal model. As regards renal revascularization, Hsu et al performed the first aortorenal bypass in a porcine model in 2000.<sup>4</sup> Eight animals were used in this study. All laparoscopic suturing and knot tying were performed intracorporeally using free-hand laparoscopic techniques exclusively. Briefly, the operative steps included:

- dissection of the aorta with cross-clamping
- transection of the left renal artery at its origin and refashioning of the proximal left renal artery
- in-situ intra-arterial renal hypothermia
- end-to-side aorto-left renal artery anastomosis
- aortic unclamping.

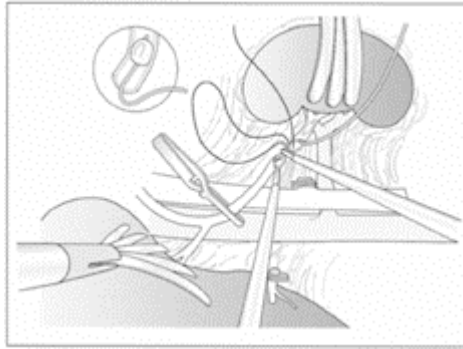


In this study, the authors also described an in-situ transarterial renal hypothermia technique to preclude loss of kidney function due to prolonged normothermic renal ischemia. For this purpose, a 4F Pruitt balloon catheter was inserted into the distal left renal artery immediately after its transection. The balloon was inflated with 0.5 ml of sterile water to occlude the arterial lumen. Continuous renal hypothermia was achieved by manually infusing icecold heparinized saline solution. The ice-cold saline was drained systemically through the intact left renal vein. To further minimize 'warm' ischemia during revascularization, cold irrigation through the Pruitt catheter was continued during the majority of the anastomotic suturing. Thus, the warm ischemia time was reduced to an acceptable 9 min even though the median time to perform the end-to-side anastomosis was 40 min. No conversion to open surgery was reported in this study. A postmortem ex-vivo angiogram demonstrated a widely patent, normal-appearing aorto-left renal artery anastomosis in all animals. In the same study, we also reported our experience with laparoscopic interposition of a synthetic graft for aortorenal revascularization. Despite a technically adequate anastomosis with intima-to-intima approximation and eversion confirmed by intraoperative Doppler ultrasonography, chronic data revealed a 100% thrombosis rate of the interposed Dacron graft. This routine occurrence of thrombosis was felt to be due to the particular incompatibility of the porcine vasculature to the synthetic Dacron graft.

### **Splenorenal bypass**

More recently, an extra-anatomic technique of renal revascularization has also been evaluated in our laboratory. Splenorenal bypass was performed on six mongrel dogs. Particularly in the canine model and unlike the clinical scenario, there is a significant disparity in the caliber of the splenic and renal arteries. Moreover, the small diameter of the distal splenic artery (2.2–2.5 mm) made this laparoscopic end-to-end anastomosis a technically challenging task. Briefly, the surgical technique comprised dissection of the distal segment of splenic artery and main left renal artery; transection and spatulation of the splenic artery and left renal artery; in-situ intracorporeal renal hypothermia; end-to-end Splenorenal anastomosis; unclamping and kidney revascularization. In-situ transarterial renal hypothermia was also achieved using a Pruitt balloon catheter as described above. However, the ice-cold solution was not drained into the systemic circulation. Instead, a laparoscopic bulldog clamp was placed on the proximal left renal vein while the stump of the left gonadal vein was incised, thus draining the perfusing ice-cold solution into the abdominal cavity.<sup>5</sup>

To overcome the limitations related to laparoscopic freehand suturing in this 'microsurgical' task, we paid particular attention to the following steps: optimal port placement, use of 3 mm needlescopic instruments, synchronization of hand movements with the animal's respiratory movements, and use of Prolene suture on an RB-2 needle. All procedures were completed laparoscopically without open conversion. On postoperative invivo/ex-vivo renal arteriogram, the anastomosis was patent in four animals, while in two animals there was obstruction of the anastomotic site. Macroscopic gross examination of these two specimens showed a narrowed



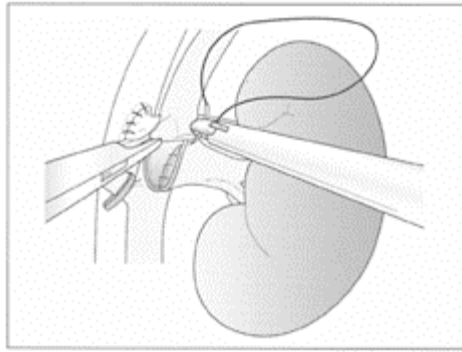
**Figure 15.1** In-situ renal hypothermia during laparoscopic Splenorenal bypass in a canine model.

thrombus within the anastomotic site in the other animal.<sup>5</sup> anastomotic site in one animal and the presence of a

### Renal autotransplantation

Renal autotransplantation is occasionally necessary for management of complex branch renal artery lesions, or for significant ureteral loss.<sup>6</sup> Performing a renal autotransplant requires two major open surgical incisions with inherent significant patient morbidity and postoperative convalescence.

Laparoscopic techniques are widely used to obtain an anatomically and functionally intact allograft for live donor transplantation. We have also used the laparoscopic approach for kidney harvesting for conventional open autotransplantation. We recently reported a laparoscopic retroperitoneal right live donor nephrectomy technique for open autotransplantation in 4 patients.<sup>7</sup> Briefly, after balloon dilation of the retroperitoneum was performed to create the initial working space, a 3-port approach was employed. Retroperitoneal live donor right laparoscopic nephrectomy was then performed. Before dividing the renal vessels, a muscle-splitting Gibson incision was made, but the transversalis fascia was left intact. Upon ligation of renal hilum, the retroperitoneum was entered through the previously made Gibson incision, and the kidney was extracted. The autograft was immediately flushed, cooled, and its vessels prepared on the bench. Standard extraperitoneal autotransplantation was performed through the same Gibson incision. Mean warm ischemia time, defined as the time from endoscopic cross-clamping of the renal artery to ex-vivo cold perfusion, was 4 min. An MAG-3 (mercaptoacetyl triglycine) renal scan on postoperative



**Figure 15.2** Free-hand laparoscopic intracorporeal suturing and knot-tying techniques were used to achieve precise vascular anastomosis during kidney autotransplant in a porcine model.

day 1 confirmed good perfusion in all autotransplanted kidneys.

In our laboratory, the next level of technical difficulty was evaluated by performing a laparoscopic renal auto-transplantation completely intracorporeally.<sup>8</sup> Following a laparoscopic left donor nephrectomy, renal hypothermia was achieved by in-situ intra-arterial perfusion of ice-cold solution. The iliac artery and vein were previously dissected in preparation for autotransplantation. Laparoscopic vascular clamps were used to individually control the iliac artery and vein. The kidney was carefully positioned and stabilized in the pelvis over the shafts of the prepositioned laparoscopic vascular clamps. Individual end-to-side anastomosis of the renal artery and vein to the common iliac artery and vein were performed precisely. At various intervals after laparoscopic autotransplantation, a laparoscopic right nephrectomy was performed in order to assess the functional status of the autograft in a solitary kidney model. Mean preoperative serum creatinine was 1.3 mg/dl, and mean serum creatinine after the staged contralateral nephrectomy was 1.6 mg/dl. Intravenous urography and aortography prior to euthanasia demonstrated prompt contrast uptake and excretion by the auto-graft and patent arterial anastomosis, respectively.<sup>8</sup>

### **Renal artery aneurysm**

Renal artery aneurysm is another surgically curable cause for renovascular hypertension. Treatment options for renal artery aneurysms include:

1. endovascular percutaneous steel coil embolization, although this alternative is limited to select patients with a small intra-renal aneurysm

2. open surgical revascularization techniques such as aneurysmectomy followed by simple arterial repair or in-situ segmental resection with end-to-end reanastomosis
3. partial or complete nephrectomy, which is an option in the presence of multiple intrarenal aneurysms.<sup>9</sup>

To our knowledge, the worldwide clinical experience with laparoscopic management of renal artery aneurysm is restricted to our 2 cases.

In the first case, a 3 cm aneurysm located at the bifurcation of the main left renal artery was completely mobilized, resected, and repaired intracorporeally. Using a 4-port transperitoneal approach, the three feeding vessels to the aneurysm were controlled individually with bulldog clamps. Circumferential mobilization of the pulsating aneurysm was the most technically challenging step of the procedure. The aneurysm sac was precisely resected, and the diameter of the main left renal artery was restored using 4-0 Prolene suture. Total operative time was 4.2 hours, blood loss was 100 ml, and the length of hospital stay was 2 days. Postoperatively, aortography revealed normal caliber of the reconstructed renal artery, with improved perfusion on renogram.<sup>9</sup>

In the second case, a 3.5 cm, trilobed, completely intrarenally located aneurysm arising from a tortuous upper pole branch of the main right renal artery was identified on a three-dimensional computed tomography (CT) scan. Due to the large dimension of the aneurysm, percutaneous steel coil embolization was ruled out. A laparoscopic upper pole partial nephrectomy was performed. A laparoscopic flexible color Doppler probe was used to identify the primary feeding vessel to the aneurysm that was clipped and transected. A Satinsky clamp was used to obtain en-bloc control of the main renal artery and vein. Cold cut scissor was employed to excise the aneurysm during upper pole heminephrectomy. Total ischemia time was 39 min, including pelvicaliceal repair and hemostasis of the renal remnant. Total surgical time was 4 hours and the patient resumed oral fluids and ambulation on post-operative day 1.<sup>10</sup>

### **Simple nephrectomy (laparoscopic retroperitoneal approach)**

Eventually, simple nephrectomy is performed for the treatment of renovascular hypertension.<sup>2</sup> In these circumstances, the kidney is usually atrophic with a diminutive blood supply, and not associated with an intense perirenal fibrosis. Therefore, these patients are ideal candidates for laparoscopic nephrectomy. A few reports on the literature have dealt with bilateral laparoscopic transperitoneal nephrectomy of native kidneys for the treatment of renin-mediated hypertension.<sup>11,12</sup> However, since the kidney is a retroperitoneal organ, a direct 'retroperitoneoscopic' approach has considerable appeal.<sup>13</sup> At the Cleveland Clinic, laparoscopic nephrectomy is preferentially performed by the retroperitoneal technique for unilateral or bilateral cases.<sup>14</sup> Notwithstanding the concerns about the smaller retroperitoneal working space, the retroperitoneal approach does offer some unique advantages, such as expeditious access to renal artery and vein and nonviolation of the peritoneal cavity, potentially decreasing the chances of inadvertent intraperitoneal organ injury and postoperative paralytic ileus.<sup>15</sup>

*Surgical technique*

With the patient secured in a full flank position, an open (Hasson cannula) technique is used to obtain initial access. A horizontal 1.5 cm skin incision is made just below the tip of the 12th rib. Using S-shaped retractors, the flank muscle fibers are bluntly separated. Entry is gained into the retroperitoneal space by gently piercing the anterior thoracolumbar fascia with the fingertip. Limited finger dissection of the retroperitoneum is performed in a cephalad direction, remaining immediately anterior to the psoas muscle and fascia, and posterior to the Gerota's fascia to create a space for placement of the balloon dilator. A trocar-mounted balloon dissection device (Origin Medsystems, Inc., Menlo Park, California) is inserted for rapid and atraumatic creation of the working space (Figure 15.3). The balloon dilation should occur in the pararenal space between the psoas muscle posteriorly and Gerota's fascia anteriorly, effectively displacing the kidney anteromedially (Figure 15.4) and thereby allowing direct access to the posterior aspect of the renal hilum.<sup>15</sup>

A caveat during retroperitoneal balloon dilation in the presence of an atrophic kidney is that there is a tendency to inflate the balloon anteriorly to the kidney, thus prematurely dislodging the kidney away from the parietal peritoneum, increases the degree of difficulty in exposing the renal hilum.

Following balloon dilatation and removal, a 10 mm blunt-tip trocar (Origin Medsystems, Inc., Menlo Park, California) is placed as the primary port. This trocar has an internal fixed fascial retention balloon and an external adjustable foam cuff, which combine to eliminate air leakage at the primary port site.

Two secondary ports are placed under 30° laparoscopic visualization. The immediately adjacent undersurface of the flank abdominal wall is visualized endoscopically. A 10/12 mm port is placed 3 fingers-breadths cephalad to the iliac crest, between the mid and anterior axillary lines. A second 10/12 mm port is placed at the lateral border of the erector spinae muscle just below the 12th rib (Figure 15.5).

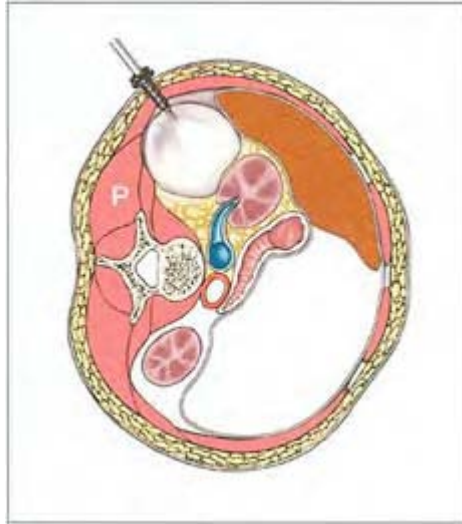


**Figure 15.3** Typically, 800 ml of air (40 pumps of the sphygmomanometer bulb) are instilled into the balloon to

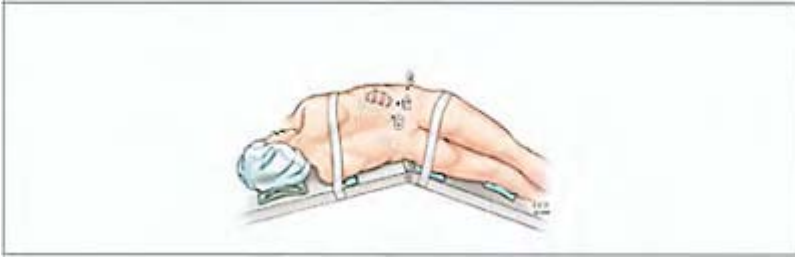
### create the initial retroperitoneal working space.

The kidney is then retracted anterolaterally with a laparoscopic small bowel clamp or the fan retractor in the non-dominant hand of the surgeon placing the renal hilum on traction. To avoid problems with orientation in the retroperitoneum, the camera should be orientated such that the psoas muscle is always absolutely horizontal on the video monitor.<sup>13</sup> Visualization of the vertically oriented, distinct arterial pulsations indicates the location of the renal artery, which is circumferentially mobilized, clipped and divided. Subsequently, the renal vein is stapled and divided with an Endo-GIA stapler (Figure 15.6). Gerota's fascia is then entered and the kidney is circumferentially mobilized within the fascia, sparing the adrenal gland. Finally, the ureter is identified, clipped, and transected.

The specimen is then placed in a bag for subsequent extraction. Since staging pathology is not an issue in these situations, piecemeal extraction can be performed using a metallic ring forceps. A small low muscle-splitting Gibson incision can be performed for intact specimen extraction. A Pfannenstiel incision at the pubic hairline is another option that further improves the cosmetic results. The latest incision is especially useful during bilateral procedures, where both specimens can be extracted through a single incision.<sup>16</sup> In these cases, it is important to maintain airtight packing of the Pfannenstiel incision during the second retroperitoneal nephrectomy to preclude intraoperative air leak.



**Figure 15.4** The distended balloon displaces kidney anteromedially, allowing access to renal vessels.



**Figure 15.5** Port placement during right retroperitoneoscopy nephrectomy. (A) Port is placed at the tip of 12th rib. (B) Port is placed at junction of lateral border of the erector spinae muscle with underside of 12th rib. (C) Port is placed 3 fingers-breadths cephalad to iliac crest, between mid and anterior axillary lines.

Alternatively, a port-site skin incision can be extended 2–3 cm to deliver significantly atrophic kidneys.

### Conclusion

Already available percutaneous endovascular techniques are highly effective with minimal morbidity for the management of renovascular hypertension. Our laboratory has investigated the applicability of laparoscopy to the management of renovascular disease. Currently, performing free-hand laparoscopic suturing in a timeefficient manner remains a challenging task. Potentially,



**Figure 15.6** Following renal artery clip-ligation the renal vein is circumferentially mobilized and secured with a gastrointestinal anastomosis stapler.

using robotic-enhanced technology to perform vascular suturing may deliver more precise movements during the vascular anastomosis. The experimental studies involving renovascular surgery summarized herein may form the basis for clinical performance of complex renovascular procedures laparoscopically in the future.

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# 16

## Renal cystic disease

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Renal cystic disease includes a variety of cystic anomalies and lesions of the kidneys and can be seen in all age groups. This chapter will include those conditions where minimally invasive options are an accepted treatment modality. A cyst is a sac lined by epithelium within the kidney. The origin for cysts could be from ectopic tubules or collecting ducts. The cysts may be continuous with the nephron or may be isolated despite a communication during pathogenesis. A majority of the cysts arise from the nephron and collecting ducts. Multicystic kidneys, however, are dysplastic kidneys that arise before the formation of the nephron. Classification of renal cystic diseases that are listed in Table 16.1 is based on the system proposed in 1987 by the Committee on Terminology, Nomenclature and Classification of the American Academy of Pediatrics (AAP), Section on Urology.<sup>1</sup>

**Table 16.1** *Classification of renal cystic disease*

*Genetic*

- Autosomal recessive (infantile) polycystic kidneys
- Autosomal dominant (adult) polycystic kidneys
- Juvenile nephronophthisis-medullary cystic disease complex:
- Juvenile nephronophthisis
- Medullary cystic disease
- Congenital nephrosis
- Cysts associated with multiple malformation syndromes

*Non-genetic*

- Multicystic kidney (multicystic dysplasia)
- Multilocular cyst (multilocular cystic nephroma)
- Simple cysts
- Medullary sponge kidneys (less than 5% inherited)
- Acquired renal cystic disease
- Caliceal diverticulum

### Simple cysts

A simple renal cyst is an oval-to-round cyst in the kidney, which is lined by a flattened cuboidal epithelium and filled with clear or straw-colored fluid. These are usually acquired lesions and are believed to originate as diverticula of the distal convoluted tubules or the collecting ducts.<sup>2,3</sup> The prevalence of renal cysts as well as the number of cysts in each kidney increases with age. The prevalence in the adult population is about 12–14%.<sup>4,5</sup> In another CT study by Tada et al, the incidence of cysts in patients by the age of 50 was at least 27%.<sup>6</sup> In a longitudinal study, the cysts were seen to increase in size at

the mean rate of 2.82 mm or 6.3% per year and cysts in younger patients progressed more rapidly than the older patients.<sup>4</sup> The ratio of men to women with renal cysts was 2:1. An autopsy study by Kissane and Smith identified a 50% incidence of simple renal cysts after the age of 50.<sup>7</sup>

Simple cysts are usually asymptomatic and incidentally detected on abdominal imaging. Occasionally, symptoms related to renal cysts include a palpable mass, pain, flank pain, and hematuria. Clinical features related to cysts can be due to infection, hemorrhage, impairment of renal function, and hypertension. Cysts can rupture into the caliceal system and cause hematuria or cause caliceal or ureteral obstruction. Cysts can also cause hypertension secondary to segmental ischemia.

### *Diagnosis*

#### **Ultrasound**

Simple cysts can typically be confirmed by a renal ultra-sonography. The characteristics of a simple cyst on ultra-sonography include a spherical smooth-walled lesion with a thin distinct margin, absence of internal echoes, through transmission of ultrasound waves through the cyst, and acoustic enhancement of the sound waves deep to the cyst. Renal cystic disease should be suspected if two or more cysts are noted in individuals 30 years or younger, or two or more cysts are noted in each kidney in those aged 30–59 years, or four cysts are noted in each kidney in those older than 60 years.<sup>8,9</sup> Other criteria are also helpful: size of the cyst, the location of the cyst, as well as the echogenicity of the cortex can also be determined via ultrasound examination. If all ultrasonographic criteria for the simple cyst are met, no further evaluation is required. However, should there be an equivocal diagnosis on ultrasound, further imaging by computed tomography (CT) or a magnetic resonance imaging (MRI) may be helpful.



**Figure 16.1** Large symptomatic simple cysts treated with aspiration and sclerotherapy. (CT courtesy of Dr Jonas Rydberg.)

**Computed tomography**

On CT imaging, apart from the distinct smooth spherical or oval thin-walled lesion seen on ultrasound, the CT lesion should be homogenous, with a density of—10 to + 20 Hounsfield units, without enhancement following intravenous (IV) contrast injection (Figure 16.1). However, CT imaging is often required in patients with complex lesions. It is important that CT be obtained with and without IV contrast and with thin sections (5 mm or less) through the kidney. When the diagnosis is equivocal, details regarding the CT technique as well as the time of imaging after injection of contrast as well as other details of technique should be determined. A hyperdense cyst can have a density of between 20 and 90 Hounsfield units but will not have enhancement after IV contrast injection. Diagnostic aspiration of the cyst is indicated only in an occasional patient, especially when an infected cyst is suspected. In patients who are poor surgical risks and when cytologic evaluation of the fluid may be helpful, cyst aspiration can be performed. MRI may be helpful, especially in identifying hemorrhagic cysts that are seen on T2 images as extremely bright lesions.

**Bosniak classification**

In 1986 Bosniak proposed a classification (Table 16.2) for renal cysts to select patients whose cysts are likely to be malignant and who would need close follow-up or surgery due to the risk of malignancy.<sup>10–13</sup> The Bosniak classification was based primarily on CT imaging to evaluate renal masses. Management decisions, however, are made on the basis of patient age and clinical conditions as well as other imaging modalities such as ultrasound and MRI.

Category I consists of simple benign cysts with CT and ultrasound features as previously described in this chapter. Category II are cysts that include one or two thin septations ( $\leq 1$  mm), fine calcification, and hyperdense cysts with homogeneously high attenuation with all other features of category I cyst. There can, however, be

**Table 16.2** *Renal cyst CT classification based on Bosniak criteria with risk of malignancy*

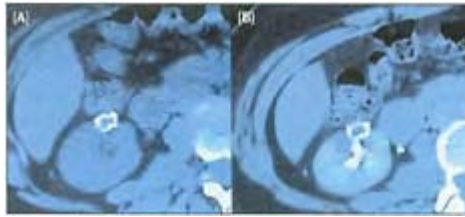
| Type | Wall                 | Septations | Calcification | Precontrast density on CT (HU) | Enhancement | Risk of malignancy | Require surgical resection |
|------|----------------------|------------|---------------|--------------------------------|-------------|--------------------|----------------------------|
| I    | Thin                 | None       | None          | 0–20                           | None        | None               | —                          |
| II   | Thin                 | None—few   | Minimal       | 0–20                           | None        | Low                | +/-                        |
| III  | Increasing thickness | Multiple   | Moderate      | 0–20                           | None        | Moderate           | +/-                        |

IV    Thick    Many    Coarse    >20    Yes    High    Yes  
 CT, computed tomography; HU, Hounsfield units. Parts of table taken from Bosniak MA<sup>10</sup> with permission.

interobserver variation in distinguishing between Bosniak II and Bosniak III lesions. Category III are complicated lesions that have more than minimal calcification and prominent septation with thicker walls or multiple septa (Figure 16.2 A, B). Category IV are clearly malignant and are considered cystic renal malignancies with irregular margins and enhancing components. Enhancement is considered significant, with an increase of at least 10 Housefield units with IV contrast.

Category I and II lesions do not require surgery; category III comprises lesions that cannot be definitively distinguished from malignant neoplasms and need to be considered for surgical exploration. Category IIF is a group not clearly defined by Bosniak and consists of lesions that do not clearly fall into the category II and require followup. Category IV are clearly considered to be radiologically malignant and require resection.

Occasionally, high-density cysts can be mistaken for enhancing renal tumors if CT imaging is performed after IV contrast alone. In these circumstances a repeated delayed CT imaging may help in differentiating between high-density cysts and solid renal neoplasms. With high-density cysts there is no change in attenuation between the initial post-contrast and the delayed CT, whereas with renal neoplasms there is a decreased attenuation in the delayed CT compared to the post-contrast CT, indicating vascularity.<sup>14</sup> Nephrotomography, renal angiography, and cyst puncture have been used in the past to differentiate the renal cysts from tumor. However, with advances in sonography, CT, and MRI, invasive procedures are rarely required for diagnostic purposes. Indications for cyst puncture include a possible renal abscess or an infected cyst, when the patient is a high risk for surgery, or when cytologic diagnosis is required for further management for the patient. In the case of an infected cyst or an abscess, percutaneous drainage after cyst puncture may be appropriate.



**Figure 16.2** (A and B) Bosniak category III cyst with thick calcified wall treated with laparoscopic wedge excision.

#### *Management of simple cysts*

Simple cysts rarely require treatment and do not need regular follow-up. Treatment for simple cysts is required if the cyst is symptomatic with pain or causes effects due to

compression of the renal parenchyma or the pelvicaliceal system. When simple cysts are to be treated, the options include aspiration, aspiration with sclerotherapy, percutaneous endocytosis, and laparoscopic decortication of cysts.

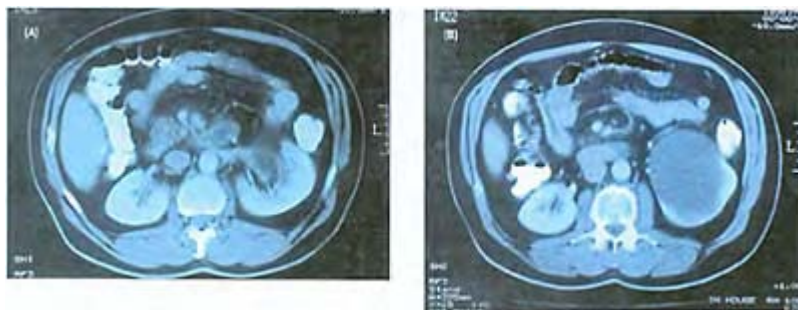
Percutaneous drainage of simple cysts is minimally invasive, is tolerated well by patients, and can be performed on an outpatient. It is typically performed under ultrasound guidance by the radiologist. However, simple aspiration does not have a high success rate, since in the vast majority of the patients the cyst persists on follow-up imaging. In a study of 156 patients there was no statistically significant difference in change of mean size between the cysts that were aspirated and the cysts that had no intervention.<sup>15</sup> In some patients in whom the symptoms may not be definitively related to the cyst, aspiration may be performed as part of the evaluation, before more invasive options such as decortication are considered if the symptoms resolve with aspiration.

### **Percutaneous aspiration and sclerotherapy**

**Indications and contraindications.** Sclerotherapy is recommended as an initial treatment of choice for simple renal cysts that are peripheral and symptomatic. Should sclerotherapy not be successful, and in those patients where sclerotherapy is contraindicated, other options should be considered. Sclerotherapy is contraindicated when the following are present or suspected: malignancy, infection, communication with the renal collecting system, and peripelvic location (Figure 16.3 A and B).

**Technique.** The treatment of symptomatic cysts with aspiration and sclerotherapy is more effective and is an effective minimally invasive option with good results. Sclerotherapy has been performed with several agents, including glucose, phenol, iophendylate, and 99% ethanol and bismuth phosphate. Other chemicals for sclerotherapy include 10% povidone-iodine and doxycycline. Ten percent povidone-iodine has also been used in combination with doxycycline.

It has been noted that a repeat injection of 99% ethanol has been more efficacious than a single injection.<sup>16</sup> In a recent study by Paananen et al, 32 patients with simple cysts were treated with ultrasound-guided percutaneous aspiration of the cysts followed by a 99% ethanol sclerotherapy.<sup>17</sup> The procedure was performed under local anesthesia with the patients hospitalized overnight. The cyst was punctured with a 15 cm 18-gauge needle under



**Figure 16.3** (A and B) This large symptomatic simple renal cyst, extending towards the pelvis of the kidney, was treated with laparoscopic decortication.

ultrasound guidance with local anesthesia. Fluid was aspirated from the cyst and sent for cytologic examination. Ten milliliters of contrast was injected under fluoroscopic guidance into the cyst after using the Seldinger technique to insert a 30 cm 5F catheter into the cyst. The fluid from the cyst was aspirated to completion. Contrast was then injected into the cyst to confirm that the cyst walls were smooth and that there was no extravasation. Ninety-nine percent ethanol was then injected into the cysts: one-fourth of the cyst volume but never more than 100 ml. The alcohol was left in the cyst for 20 min and the patient rolled from side to side in different positions at intervals of 5 min. Following this, all the alcohol was aspirated. The cyst was similarly treated once or twice more during the same session. Twenty milliliters of 2% lidocaine hydrochloride has been injected into the cyst for 15 min before the alcohol injection in order to relieve the pain that can sometimes be associated with alcohol sclerotherapy. Other investigators<sup>18</sup> have used 95% alcohol sclerotherapy with three doses at intervals of 24 hours. Alcohol is rarely absorbed through the cyst wall, with detectable levels of alcohol in the urine and blood.

**Results:** Sclerotherapy with ethanol was successful in the disappearance of the cyst in 22% of cases, and mean size of all cysts decreased from 7.8 cm to 1.7 cm, with a mean follow-up of 55 months. There was no correlation between the size of the cyst and intensity of the pain.<sup>17</sup> Sclerotherapy with bismuth phosphate has also been effective in the treatment of simple renal cysts.<sup>15</sup> Fifty percent acetic acid has also been used for sclerotherapy and in one study was noted to induce faster and more complete regression of the cyst compared with 99% ethanol.<sup>19</sup>

### Ureteroscopic approach

Ureteroscopic marsupialization is suitable for small or medium-sized parapelvic and centrally located cysts.<sup>20</sup> This approach can be considered in patients who are poor candidates for more invasive surgery. The flexible ureteroscope can be used to incise the wall of the cyst to allow adequate drainage into the collecting system. Fluoroscopy with retrograde pyelography and ultrasound may be used to assist with localization of the cyst. Electrosurgical energy or a holmium laser can be used to perform a cruciate incision in the cyst wall.

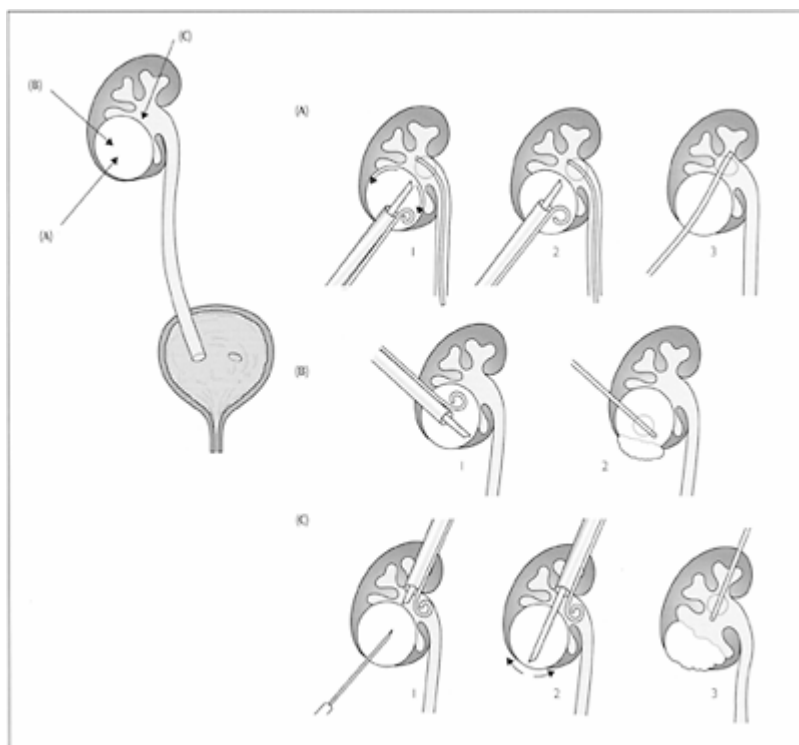
### Percutaneous endocystolysis

There have been a few reports of percutaneous decortication of renal cysts.<sup>21–23</sup> This approach involves general anesthesia but is less invasive than the laparoscopic approach.

**Indications and results.** An ideal patient for this approach is one who has a medium-sized or large solitary posterior cyst, preferably in the mid or lower parts of the kidney. Long-term follow-up of 10 patients who underwent percutaneous resection of renal cysts was reported by Plas and Hubner in 1993.<sup>23</sup> All patients were cured of symptoms without late complications, with a median follow-up of 45.7 months. The cysts had completely resolved in 50% of patients. Cyst recurrence was seen in 30% and there was a 45% decrease in cyst size in 20% of patients. The technique described by Kang and colleagues has been successful in 9 patients with a mean follow-up of 21 months.<sup>21</sup> Eight of 9 patients had complete resolution of pain and 1/9 had significant improvement in pain. Follow-up CT imaging revealed complete or near-complete resolution in 7 patients and small cysts in 2 patients.

**Technique.** The patient is initially placed in the lithotomy position and a retrograde pyelogram is performed (Figure 16.4). An open-ended ureteral catheter is placed with its tip in the renal pelvis to facilitate injection of indigo carmine solution during the percutaneous procedure.

The patient is then turned to a prone position for the percutaneous cyst decortication. The cyst is localized using fluoroscopy with injection of contrast via the retrograde catheter. Ultrasound may also be used to help localize the cyst accurately and to direct the percutaneous access. A 15 cm 18-gauge needle is used for percutaneous direct access into the cyst. Cyst fluid is aspirated and sent for cytologic examination. An 80 cm J wire is passed through the needle before the needle is removed. The percutaneous



**Figure 16.4** Three approaches for percutaneous access for cyst decortication. (A) Direct approach: (1) cyst is punched directly and cyst wall is incised into the pelvis; (2) cyst wall is fulgurated; (3) a nephrostomy tube is placed through the cyst. (B) Direct approach through parenchyma: (1) cyst is punctured through the parenchyma; (2) a nephrostomy tube is placed in the cyst—no communication between the cyst and the collecting system. (C) Indirect approach: (1) collecting system is entered first and cyst is punctured and distended for easy identification; (2) cyst wall is fulgurated; (3) a nephrostomy tube is placed, (from Clayman et al.<sup>24</sup>)



tract is dilated over the wire with a balloon dilator to 30F after a second safety guide wire is inserted into the cyst. A 26F rigid nephroscope with an offset lens and a straight working channel is used with glycine irrigant. After initial inspection of the cyst, a 26F resectoscope with a rollerball electrode is used. The lining of the cyst is gently fulgurated with a rollerball electrode. After the cyst wall is fulgurated, a portion of the cyst wall is marsupialized into the retroperitoneum with a grasping forceps. Indigo carmine injected into the collecting system helps identify the cyst wall facing the retroperitoneum. Care is taken to limit the extravasation of glycine into the retroperitoneum to avoid the transurethral resection (TUR) syndrome.

The other percutaneous approach to the cyst is via a direct approach but through adjacent renal parenchyma. The cyst is marsupialized into the retroperitoneum but not into the collecting system. The third approach is an indirect method where percutaneous access is achieved into the collecting system at a site distant to the cyst. After dilation of the tract and insertion of a 30F Amplatz sheath, the cyst is marsupialized into the collecting system. Before the cyst is marsupialized in this manner, an 18 gauge needle is inserted percutaneously into the cyst and saline injected into the cyst to facilitate visualization of the cyst wall to the nephroscopist.<sup>24</sup>

### Laparoscopic decortication

**Indications.** For laparoscopic cyst decortication, indications include:

1. simple cysts that have failed aspiration with sclerotherapy
2. cysts with close proximity to the collecting system (see Figure 16.3A and B) or with a possible communication with the collecting system
3. peripelvic cysts (Figure 16.5)



**Figure 16.5** Peripelvic cyst is a contraindication for sclerotherapy.

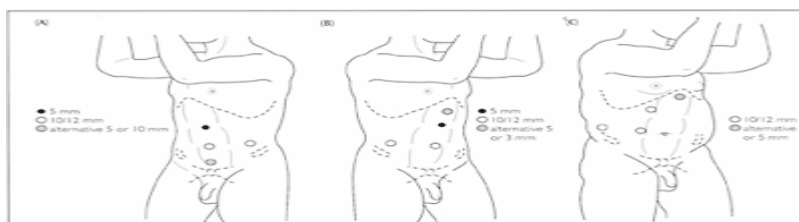
4. cysts that are suspicious for malignancy or where malignancy cannot be definitively be ruled out
5. autosomal dominant polycystic kidney disease.

Laparoscopic cyst decortication can be performed via a transperitoneal or a retroperitoneal approach. For simple cysts, the approach can be dictated by the location of the dominant cyst using a retroperitoneal approach for a more posterior cyst and a transperitoneal approach for a more anteriorly placed cyst.

**Preoperative preparation:** The patient is placed on a liquid diet and given a Fleet's enema the night before the surgery and a bottle of magnesium citrate about 24 hours before surgery. IV cefazolin is administered preoperatively for antibiotic prophylaxis. Should there be suspicion of infected cysts, especially in patients with autosomal dominant polycystic kidney disease, an IV fluoroquinolone such as ciprofloxacin is administered to achieve adequate antibiotic levels within the cyst. Preoperatively, a ureteral catheter is placed in selected patients, such as those with autosomal dominant polycystic kidney disease and with peripelvic cysts. In these patients, access to their retrograde ureteral catheter is maintained to facilitate injection of indigo carmine during the surgery to confirm that no caliceal violation has occurred. In these instances, if a small caliceal injury is noticed the ureteral catheter is used at the end of the procedure to pass a guide wire in a retrograde fashion to insert an indwelling double pigtail ureteral stent under fluoroscopic guidance to drain the collecting system.

**Patient positioning:** The patient is positioned in a lateral decubitus position with the table flexed. The patient is anchored securely to the table and all bony prominences are well padded to ensure that there is no neuromuscular injury as a result of positioning. Pneumatic compression stockings are applied before the patient is positioned.

**Port placement:** Pneumoperitoneum is established in the left lower quadrant using the Veress needle or the dilating trocar with the visual obturator (Ethicon Endopath 12 mm trocars). A 2nd 12 mm trocar is inserted at the umbilicus. In obese patients this trocar is inserted at the lateral border of the rectus abdominis muscle. The 3rd trocar is a 5 mm trocar that is inserted in the midline midway between the umbilicus and the xiphisternum. The 4th trocar may occasionally be required if lateral retraction of the kidney is required. This is a 5 mm trocar that is inserted in the subcostal region along the anterior axillary line (Figure 16.6A). If access to the upper pole is required on the right side, an additional 5 mm trocar is inserted medially in the subcostal region to help retract the liver away from the superior pole of the kidney.

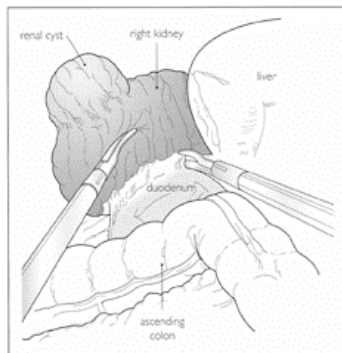


**Figure 16.6A** Trocar site placements.

Two 10/12 mm trocars are placed: one at umbilicus and one at the level of umbilicus lateral to the edge of rectus muscle. A 5 mm trocar is placed in the

midline between umbilicus and the xiphoid process. An additional 5 mm trocar can be inserted medially in the subcostal region. (A) Left-sided procedures. (B) Right-sided procedures. (C) In obese patients, all trocars are shifted laterally.\*

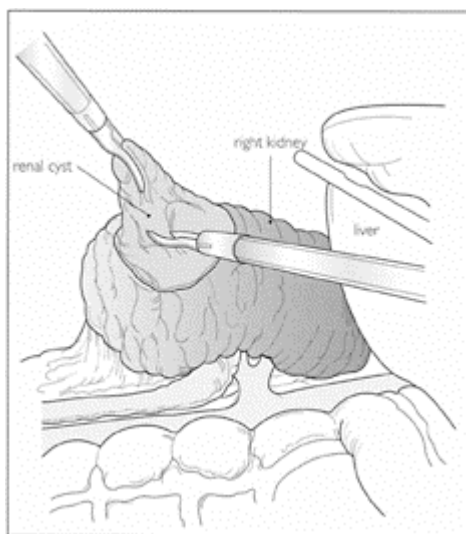
**Technique:** The line of Toldt is incised with a Harmonic Scalpel (Ethicon Endo-Surgery, Inc., Cincinnati, Ohio) and the colon is mobilized medially off the Gerota's fascia (Figure 16.6B). The Gerota's fascia is dissected off the surface of the cyst. The perinephric fat and Gerota's fascia around the cyst is excised in order to expose the entire cyst as well as a normal renal parenchyma surrounding the cyst. Initially, it is preferable not to decompress the cyst in order to dissect the margins completely. However, should the size of the cyst be impeding complete dissection of the cyst, it can be aspirated with a spinal needle to decrease the size. In the case of a simple cyst, the cyst fluid is first aspirated. The wall of the cyst is excised flush with the renal parenchyma and sent for histopathologic examination (Figure 16.6C). The base of the cyst is then inspected and, should there be any suspicion, biopsies of the base are obtained. The biopsy sites would need to be fulgurated in order to obtain adequate hemostasis. The cyst wall that is attached to the renal parenchyma can be fulgurated to prevent recurrence; however, this should be avoided if there is a risk of injury to the collecting system, depending on the preoperative imaging.<sup>25</sup> Once the cyst has been decorticated, perirenal fat can be placed and secured in place to help prevent reaccumulation. Polytetrafluoroethylene wick has also been used for a large peripelvic cyst.<sup>26</sup> We do not routinely recommend a drain in patients with a simple cyst (Figure 16.6D).



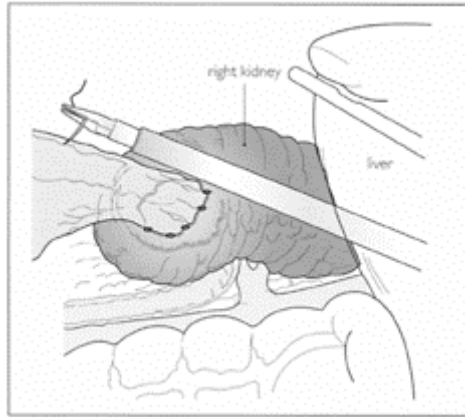
**Figure 16.6B** Laparoscopic renal cyst decortication. Mobilization of colon and duodenum to free up Gerota's fascia. Sharp dissection with

laparoscopic scissors prevents the possibility of bowel injury. An exophytic cyst can usually be identified or laparoscopic ultrasound can be used. Gerota's fascia is then dissected off the surface of the cyst.\*

\* (From Fabrizio MD. Laparoscopic evaluation and treatment of symptomatic and indeterminate renal cysts. In: Bishoff JT & Kavoussi LR (eds). Atlas of Laparoscopic Retroperitoneal Surgery. Philadelphia, PA: WB Saunders Company, 2000.)



**Figure 16.6C** Laparoscopic renal cyst decortication. Cyst fluid is first aspirated. Then the wall of the cyst is excised flush with renal parenchyma and sent for histopathologic examination. The base of the cyst is then inspected and biopsied if indicated. The base of the cyst is then fulgurated.\*



**Figure 16.6D** Laparoscopic renal cyst decortication. Decorticated perirenal fat or a piece of omentum can be sutured and secured in place.\*

### Peripelvic cysts

Peripelvic cysts may be more difficult to treat laparoscopically because of their close relationship to the hilar blood vessels (see Figure 16.5). In these patients, depending on the location of the cysts, it may be necessary to dissect the renal hilar vessels to prevent hemorrhage during cystic cortication. Fluid is aspirated and sent for cytologic analysis. The entire cyst wall may not be accessible for excision. In these circumstances, the cyst wall is excised in those accessible locations between the hilar blood vessels. The cyst wall remnant is not fulgurated because of its proximity to the renal pelvis and hilum. The cyst cavity is then filled with perinephric fat or a polytetrafluoroethylene wick. A 10 mm laparoscopic ultrasound probe (B-K Medical, Copenhagen, Denmark) with a flexible and steerable tip is valuable for peripelvic cysts and other cysts that are not readily visible on the surface of the kidney. The laparoscopic ultrasound probe is inserted through a 12 mm port and has ability to control the angulation of the tip. Should adequate contact between the renal surface and the ultrasound probe not be obtained, irrigation with saline within the abdomen can help with ultrasound visualization.

### Indeterminate renal cysts

In the majority of patients with indeterminate cysts where surgical exploration is indicated a laparoscopic partial nephrectomy is feasible and safe. This is especially true with patients with small cysts that are exophytic and peripheral. Rarely it may be necessary to further evaluate the cyst before a decision on excision is made. This is especially true in larger indeterminate cysts where confirmation of malignancy may necessitate a radical nephrectomy. In these rare instances the cyst may be aspirated and the fluid sent for cytology. The cyst wall is also excised and a biopsy of the floor of the

cyst performed; further management is based on the results of the frozen section pathology evaluation. If the cyst is confirmed to be benign, the edges of the cyst remnant are fulgurated. Although there is a theoretical risk for dissemination of malignant cells within the abdomen, this has not been reported by the authors.<sup>27,28</sup> If the frozen section pathology confirms malignancy, a radical or partial nephrectomy is performed, depending upon the size and location of the tumor and the patient's renal function and medical condition.

In a recent series of 35 patients with indeterminate renal cysts who were treated with laparoscopic exploration as described, 14% were found to have cystic renal cell carcinoma. There was no evidence of local recurrence or distant metastases with a mean follow-up of 20.2 months.<sup>27</sup>

\* (From Fabrizio MD. Laparoscopic evaluation and treatment of symptomatic and indeterminate renal cysts. In: Bishoff JT & Kavoussi LR (eds). *Atlas of Laparoscopic Retroperitoneal Surgery*. Philadelphia, PA: WB Saunders Company, 2000.)

### **Autosomal dominant polycystic kidney disease**

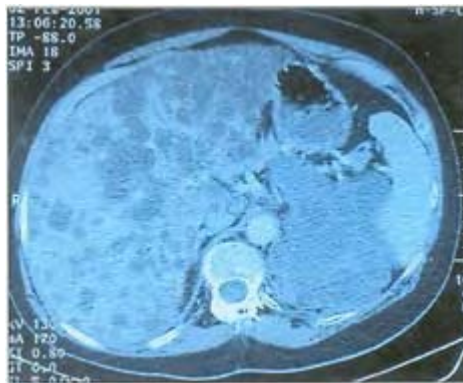
Autosomal dominant polycystic kidney disease (ADPKD) is an inherited disorder which accounts for 10–15% of patients who are on hemodialysis.<sup>29</sup> It is characterized by multiple bilateral renal cysts (Figure 16.7) and can result in progressive renal failure. It is seen in 1:500–1000 patients and over 500,000 Americans have been diagnosed with ADPKD.<sup>30</sup> Most patients are diagnosed to have ADPKD between the ages of 30 and 50 years old, although the condition is also diagnosed occasionally in children. Two genes have been implicated with the genesis of ADPKD. These are the PDK genes: PDK-1, which is on the short arm of chromosome 16, and PDK-2, which is on chromosome 4. PDK-3 is also seen in a small percentage of patients who do not have PDK-1 or PDK-2.<sup>31</sup>

Other manifestations of ADPKD include hepatic cysts (Figure 16.8), cerebral aneurysms, mitral valve prolapse, and chronic diverticulosis. Hepatic cysts may be seen in about 60% of patients.<sup>32</sup> However, these cysts rarely are symptomatic. Rarely, they can lead to portal hypertension. Occasionally, large hepatic cysts may need decortication during renal cyst surgery.

Symptoms and signs of the disease typically occur between the ages of 30 and 50 years old.<sup>33</sup> Symptoms include hematuria, flank pain, and gastrointestinal symptoms. Hypertension is also a major presenting sign, while 20–30% of patients with ADPKD can develop renal stones.<sup>34</sup> Pain can be related to cyst size.<sup>35</sup> In a study by Hatfield and Pfister, over 50% of symptomatic patients had cysts over 3 cm in size, but they were present in only 20% of asymptomatic patients.



**Figure 16.7** Patient with ADPKD (autosomal dominant polycystic kidney disease) and renal pain who underwent laparoscopic left renal cyst decortication.



**Figure 16.8** Hepatic cysts in this patient required hepatic cyst decortication during laparoscopic renal cyst decortication.

About 64% of patients with ADPKD develop microscopic or gross hematuria.<sup>36</sup> Most episodes of hematuria are due to urinary tract infections or renal cyst rupture and urolithiasis. However, other conditions can coincidentally occur with ADPKD, and therefore hematuria must be investigated in order not to miss other conditions such as upper tract malignancy or bladder carcinoma. Gross hematuria can be seen in as many as about 50% of patients with ADPKD. Hematuria is generally self-limiting and lasts

generally for 7 days; it resolves spontaneously with conservative management, such as bed rest, IV hydration, and narcotic analgesics.

### *Diagnosis*

It is usually not difficult to differentiate between localized cystic renal conditions and autosomal dominant polycystic kidney disease. Renal cysts in ADPKD are bilateral and involve both the cortex and medulla. Usually, however, ADPKD can have a symmetric onset, especially in children. In some patients with unilateral nonprogressive localized cystic disease and multiple simple cysts, it may be difficult to differentiate between ADPKD and localized cystic disease. In these patients, long-term follow-up, family history, and imaging of other family members may confirm the diagnosis. ADPKD is often associated with cysts of the liver and pancreas and in a small percentage of patients cerebral aneurysms can also be seen. Localized cystic disease of the kidney comprises multiple cysts in one portion of the kidney, which could be mistaken for a polycystic kidney, multilocular cystic nephroma, or cystic neoplasm. The parenchyma between the cysts have enhancement that is similar to the enhancement in the rest of the renal parenchyma. Also, there is no encapsulation of the cystic mass, as can be seen in neoplasms. In addition, there are often discrete cysts in the rest of the kidney that are not within this cystic lesion.

It is important to obtain a family history of ADPKD when evaluating patients with bilateral renal cysts. If no family history is obtained, a proper diagnosis can still be made in patients with bilateral cysts if two or more of the following symptoms are seen:

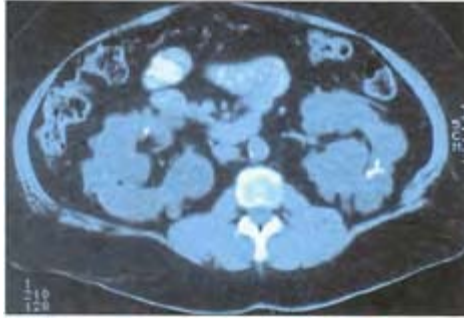
1. bilateral renal enlargement
2. three or more hepatic cysts
3. cerebral artery aneurysm
4. solitary cysts of the arachnoid, pineal gland, pancreas, or spleen.<sup>37</sup>

Before laparoscopic decortication, imaging should rule out solid suspicious lesions. Renal ultrasound and CT scan with and without IV contrast is usually adequate. However, in patients with renal impairment, an MRI with IV gadolinium may be required.

### *Urolithiasis*

Urolithiasis occurs in about 20% of patients with ADPKD and is 5–10 times more frequent in those patients compared with the general population (Figure 16.9).<sup>36,38</sup> Uric acid stones constitute the majority of stones seen in patients with ADPKD, although other stones such as calcium oxalate, calcium phosphate, calcium carbonate and struvite are also seen.<sup>36,39</sup> Stone formers amongst ADPKD patients have larger cysts compared with non-





**Figure 16.9** CT of a patient who had undergone renal transplantation for renal failure with ADPKD (autosomal dominant polycystic kidney disease) and presented with bilateral Urolithiasis and recurrent UTIs (urinary tract infections) from the native kidneys. She was treated with hand-assisted laparoscopic bilateral nephrectomy.

stone formers. Increased cyst numbers are also associated with stone formation. It is therefore possible that urinary stasis related to larger cysts and increased number of cysts contributes to stone formation. Causes of stone formation in ADPKD include tubular dilation, urinary stasis, and metabolic abnormalities. High incidences of hypocitraturia and hyperuricosuria have been reported by Torres and associates.<sup>38</sup>

Treatment options for patients with ADPKD are similar to patients without ADPKD, depending on the stone size, location, and caliceal anatomy. Shock wave lithotripsy (SWL), ureteroscopy, and percutaneous nephrolithotomy (PCNL) have therefore been used for ADPKD.<sup>40,41</sup> In a multicenter report of 20 patients from 6 centers, SWL and PCNL were used in 16 and 4 patients, respectively. The stone-free rate was 43% and 80%, respectively, following lithotripsy and percutaneous nephrolithotomy.<sup>42</sup> In another report of 16 renal units, 13 were treated with SWL and 3 with open surgery. The overall stone-free rate was 85% at 3 months, including patients who underwent repeat lithotripsy.<sup>41</sup> Percutaneous nephrolithotomy in patients with ADPKD is performed rarely. However, this approach can be used with larger stones such as stag horn stones. Open surgery is rarely required in the contemporary management of Urolithiasis in ADPKD patients.

*Management of pain in patients with autosomal dominant polycystic kidney disease*

Pain in patients with ADPKD can be multifactorial in etiology. Apart from the pain due to urologic conditions such as Urolithiasis, cyst enlargement, cyst rupture, and hydronephrosis, other causes of chronic pain can be a complex problem in these patients. Mechanical back pain can result from increased lumbar lordosis and degenerative changes in the spine.<sup>43</sup> When obvious causes for renal pain are excluded, an MRI of the spine in these patients should be performed in order to rule out disc disease or other spinal abnormalities, such as spinal stenosis and lumbosacral radiculopathy due to disc disease or degenerative spine disease. Appropriate management of the spinal pathology can relieve pain in these patients.

Renal pain in these patients can result from compression of cysts on the surrounding tissues, traction on the pedicle of the kidney, and distention of the capsule. The severity of pain generally correlates with the size and number of the cysts, but there can be exceptions. Often there is a renal and an extrarenal component to the pain. A comprehensive approach to management of pain in these patients should be formulated in conjunction with the nephrologist and the pain clinic. Treatment options for pain in ADPKD patients include physical measures, psychobehavioral modifications, systemic analgesics, physical therapy and interventions such as transcutaneous electrical nerve stimulation (TENS), acupuncture, autonomic plexus blockade, neuromodulation by spinal cord stimulation, neuroaxial, opioids, and local anesthetics. Analgesics that have been successfully used include acetaminophen, salsalate, nonsteroidal analgesics, COX-2 (cyclooxygenase 2) inhibitors, tramadol and clonidine, before trying opioids with or without clonidine.<sup>43</sup> After conservative treatments have failed, surgical options must be considered. Aspiration of the cysts is not successful, since this is usually followed by rapid reaccumulation of fluid and recurrence of pain. Bennett et al reported that only 33% of patients who were treated with ultrasound-guided aspiration of cysts were pain-free at 18 months compared with 81% treated with open cyst decortication.<sup>44</sup>

*Cyst decortication*

## Results

The original surgical decortication of renal cysts was performed by Rovsing in 1911.<sup>45</sup> Cyst decompression was performed by other authors who claimed considerable success. However, in 1957, after a report by Bricker and Patton suggested that patients who underwent surgical decompression of polycystic kidneys develop worsening of renal function, this procedure was abandoned for several years.<sup>46</sup> There were also a considerable morbidity and mortality in these patients after surgery during that time.<sup>47</sup> In the 1980s, however, surgical cyst decortication in ADPKD patients was rediscovered with encouraging results.<sup>44,48</sup> In 1992 Elzinga and colleagues reported a group of patients who were prospectively studied after undergoing 32 cyst decompression or decortication operations.<sup>49</sup> They reported up to 80% success 12 months postoperatively and 62% at 24 months following surgery. They also found that among patients following pain relapse

the pain was often lessened and fewer patients were taking analgesics in comparison with the preoperative group. More importantly, no deterioration in renal function was observed postoperatively.

With the introduction of urologic laparoscopy in the 1990s there have been several reports of decortication of cysts. In 1995 Teichman and Hulbert reported 6 cases of laparoscopic cyst decortication (LCD) of patients with ADPKD.<sup>50</sup> With a follow-up of 6–40 months, pain relief was achieved in all patients but one, who underwent renal and hepatic cyst decortication. Brown and associates from the Mayo Clinic reported LCD in 13 patients (8 with ADPKD), with 62% of the patients having good pain relief 12–28 months postoperatively.<sup>51</sup> Twenty-nine patients who underwent 35 LCD procedures were meticulously followed prospectively at Washington University with a mean follow-up of 32.3 months.<sup>52</sup> At 12, 24, and 36 months, 73%, 52%, and 81% of patients, respectively, noted a greater than 50% improvement in pain. The mean operating time was 4.9 hours and a mean of 220 cysts (range=4–692) were treated in each patient. More importantly, the majority of patients had improvement in their hypertension and the procedure was not associated with worsening renal function. LCD in patients with ADPKD is performed primarily for refractory pain caused by enlarged kidneys to multiple cysts. Surgery is also indicated in patients whose renal enlargement causes significant abdominal distention and discomfort. Percutaneous aspiration of cysts has not been successful in the long term. LCD is therefore an acceptable option for patients with enlarging cysts that require surgery.

### **Preoperative preparation**

Patients with renal pain could also have cyst infections. Lipid-soluble antibiotics such as fluoroquinolones are useful in penetrating the cyst wall. Other antibiotics that are also lipid soluble include trimethoprim-sulfamethoxazole and chloramphenicol.<sup>53</sup> Patients receive bowel preparation, and patient positioning and trocar placement are similar to that described for cyst decortication of simple cysts.

### **Technique**

Cyst decortication can be performed laparoscopically via a transperitoneal or retroperitoneal approach. We prefer the transperitoneal approach for laparoscopic surgery in patients with ADPKD because of the greater operating space that is available with this approach. Occasionally, patients with hepatic cysts can also undergo simultaneous hepatic cyst decortication via the laparoscopic approach.

When obtaining pneumoperitoneum with a Veress needle or with dilating trocar, it is important that the CT scan be reviewed in order not to insert the trocar or the Veress needle into the kidney itself. This is an important consideration when dealing with polycystic kidneys that can occupy the entire abdomen and can extend into the lower quadrant. The open approach (Hassan) to obtaining a pneumoperitoneum after insertion of the primary port is an option for the inexperienced laparoscopist and when the entire lateral abdomen is distended with the hugely enlarged kidney.

The line of Toldt is incised and the colon is mobilized off the Gerota's fascia. The plane between the Gerota's fascia and the mesocolon is developed until the colon is

mobilized entirely. The colonic mobilization is continued until the hilum of the kidney is exposed in order to access the majority of the cysts. The perinephric fat is usually attenuated in patients with ADPKD. The Gerota's fascia is dissected off the anterior surface of the kidney to expose the majority of the cysts.

The cysts in the lower pole of the kidney are first drained to allow adequate mobilization of the upper pole. The superficial walls of the larger cysts are excised and sent for histopathologic examination. The medium cysts are treated with cruciate incisions on the roof, and the smaller cysts are punctured and drained. The decortication of the cysts is performed with the harmonic scalpel, the hook electrode, or the Endo-shear. Hemostasis is achieved with meticulous cauterization of the edges of the excised cysts with electrocoagulation. Indiscriminate electrocoagulation of the interior of the cyst is avoided to prevent caliceal entry. Incision into the renal parenchyma adjacent to the cyst is avoided to prevent excessive bleeding. The argon beam coagulator is used as required. In this manner the entire anterior wall of the renal cyst is treated. The hilum is dissected in order to be able to treat the cysts in the hilar region without vascular injury. After the superficial cysts have been treated, the retrograde injection of indigo carmine helps to distend and identify the renal collecting system, as previously described in this chapter.

After treating the entire anterior surface of the kidney, the kidney is mobilized in order to expose the posterior surface. The cysts in the posterior surface of the kidney are similarly treated. Complete mobilization of the kidney is essential to decorticate all visible cysts. Incision of the coronary ligament of the liver may be necessary to expose the superior aspect of the right polycystic kidney. A 10 mm flexible ultrasound probe is used to identify the cysts that are not obviously visible and deeper within the kidney parenchyma. Depending on the mobility of the kidney at the end of the procedure, the kidney may need to be fixed to the posterior abdominal wall with 2.0 polyglactin

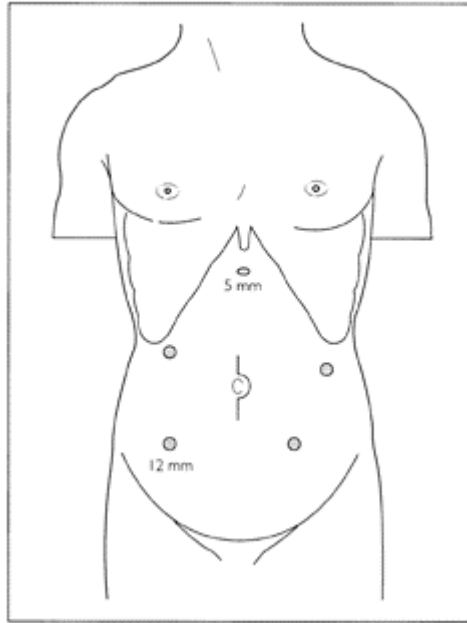
sutures using intracorporeal laparoscopic suturing.<sup>54</sup> At the end of this procedure it is important that the peritoneum be irrigated with at least 1 liter of saline to ensure that the cyst fluid that has spilled into the peritoneum be evacuated. Certain cyst fluid can cause peritoneal irritation, leading to significant postoperative pain. Peritoneal drainage is not required. Intra-abdominal pressure is decreased to 5 mmHg to ensure that there is no bleeding. The trocars are then removed under vision. When a bladed trocar is used, the 10 and 12 mm trocar sites are closed using 0 polyglactin sutures, utilizing the Carter-Thomason device. The skin at the trocar sites is closed using 2-octyl Cyanoacrylate (Dermabond; Ethicon, Inc, Somerville, New Jersey) skin adhesive. After the skin edges are clean and dry, they are held together and the Dermabond is applied with light brush strokes. At least three layers of the adhesive are applied.

### **Bilateral nephrectomy**

Patients who are in end-stage renal failure, on hemodialysis, or who have undergone renal transplantation occasionally require unilateral or bilateral nephrectomy for chronic abdominal pain (see Figure 16.8) or symptoms related to significant abdominal distention. Bilateral nephrectomy for ADPKD can be performed via a transperitoneal or a retroperitoneal approach. We prefer a transperitoneal approach because of the increased space as well as the easier specimen extraction with that approach. It is essential to

carefully image these patients preoperatively before cyst decompression is performed, since incidental renal tumors may be seen in these patients and cyst decortication in this situation can cause tumor spillage.

In a recent report by Rehman et al from Washington University, 3 patients underwent bilateral hand-assisted laparoscopic nephrectomy.<sup>55</sup> Bilateral nephrectomy can be performed with a single hand assisted device placed via a periumbilical incision (Figure 16.10). Two additional



**Figure 16.10** Port placement for laparoscopic hand-assisted bilateral nephrectomy for a right-handed surgeon. The lower 12 mm ports are used for the laparoscope and a periumbilical incision is made for the hand-assistance device. An additional 5 mm port may be used in the anterior axillary line for lateral retraction of the kidney during hilar dissection.

12 mm ports and a 5 mm port are then inserted on each side to perform the bilateral nephrectomy. The patient can be placed in a lateral decubitus position and the position changed after one side is performed. We use the beanbag, which supports the patients laterally on both sides. The patient is then strapped to the table securely with adequate

padding at bony prominences. With this arrangement, the patient can be rotated about 40–50° in each direction, in order to elevate the ipsilateral side and perform the operation without having to reposition the patient after the first nephrectomy is performed. Hand assistance in this operation considerably reduces the operating time and is recommended, especially since an incision will have to be made to extract the specimen. The midline incision is adequate for hand assistance on both sides as well as to extract both kidneys.

After initial colonic mobilization, some of the cysts may need to be decompressed in order to facilitate hilar dissection. After the hilar vascular control is obtained, further cyst decortication may be required in order to facilitate the delivery of the specimen to the hand-assist device incision. With a periumbilical incision the left hand can be used for both sides for the right-handed surgeon. Several devices are available for hand assistance. Each device has its own advantages and disadvantages. We have recently used the Lap Disc (Ethicon Endo-Surgery, Cincinnati, Ohio) as well as the GelPort (Applied Medical Resources, Rancho Santa Margarita, California) effectively.

These patients are generally at the higher risk for perioperative complications, since they are typically on dialysis or have had renal transplantation, and are on immunosuppressant medication including steroids. The peritoneum is thoroughly irrigated with saline, since some of the cysts are decompressed before extraction of the specimen. Cyst decortication can cause considerable peritoneal irritation and postoperative pain. To minimize this, some of the cysts can be drained after the lower pole is delivered outside the abdominal incision. With the drainage of cysts outside the abdomen with a partially extracted kidney, peritoneal irritation can be avoided or minimized.

Bilateral nephrectomy has also been performed for ADPKD via a retroperitoneal approach.<sup>56</sup> With the retroperitoneal approach, the patient is placed in the full lateral position and securely strapped to the table. The table is flexed in order to maximize the distance between the costal margin and iliac crest. Access is gained in the retroperitoneal approach using a 1.5 cm incision off the tip of the 12th rib. Balloon dilation is performed with 800–1000 ml of air. Three 12 mm trocars are used: one off the tip of the 12th rib; another 12 mm port at the junction of the lateral erector spinae muscle and the 12th rib; and another 12 mm port 3 cm cephalad to the iliac crest. After the nephrectomy is performed via a standard retroperitoneal approach, a lower midline incision is made 12 cm long. Blunt dissection is performed in a posterolateral direction, posterior to the rectus abdominus muscle, in order to reach the retroperitoneal space containing the kidney that was previously removed via a retroperitoneal approach. This approach avoids peritoneal violation and the complications associated with it. However, retroperitoneal nephrectomy with a massively enlarged kidney in a limited space can be technically challenging and is recommended only for surgeons with extensive experience with this approach.

### **Hydatid cyst**

Hydatid cysts are parasitic cysts that are associated with echinococcal infestation. Although rare in the continental United States except Alaska, this microorganism is still prevalent in the regions such as the Middle East and Australia. Silber and Moyad<sup>57</sup> described three forms of the disease:

1. a benign sylvatic form of *Echinococcus granulosus* endemic to Alaska, where the renal lesion is a calcified unilocular cyst
2. a pastoral form of *E. granulosus*, where the cyst expands rapidly and can rupture
3. *E. multilocularis*, which, although uncommon, is invasive with a high mortality rate.

The most common symptom is flank pain.<sup>58</sup> Other symptoms are hematuria, malaise, fever, and hydatiduria. Eosinophilia can be present and occasionally daughter cysts can be seen in the urine. The Casoni skin test, the Weinberg (complement fixation) test, and the indirect hemagglutinin test may be helpful in making the diagnosis. Imaging may reveal a calcified cystic renal lesion. CT imaging can detect calcification and the daughter cysts, as well as extrarenal involvement. If the kidney is extensively involved and poorly functioning, a laparoscopic nephrectomy can be performed. Care should be taken during the nephrectomy to avoid spillage of cyst contents into the abdomen, since seeding with daughter cysts can occur.

Partial nephrectomy or total nephrectomy is performed depending upon the size and location of the cyst and the function of the kidney. Intra-operative spillage of cyst contents can be a serious complication. LCD has been described when the cyst is small and the kidney has good function. The retroperitoneal laparoscopic approach is preferred if the cyst is accessible via the retroperitoneal approach. The cyst is exposed and the cyst contents aspirated. The cyst cavity is then filled with dilute povidoneiodine and drained. The cyst is then decorticated, as described for simple cysts. The retroperitoneum is thoroughly irrigated with saline.<sup>59</sup> Other scolecidal agents include 30% saline, 2% formalin, 1% iodine, and 0.5% silver nitrate.

## Conclusion

Renal cystic disease can be managed with a variety of minimally invasive options. A thorough evaluation with radiologic imaging is essential to make the initial diagnosis in order to differentiate malignant from the nonmalignant cystic conditions. In the vast majority of patients a definitive diagnosis can be made without the need for invasive interventions such as angiography or aspiration. A few indeterminate complex cysts may require surgical exploration and resection.

Simple cysts rarely require treatment and are often incidental radiologic findings. When simple cysts are symptomatic they can be managed in most cases with aspiration and sclerotherapy. When sclerotherapy fails or is contraindicated, LCD is effective. Other options in selected patients include the ureteroscopic and percutaneous approaches. Laparoscopic decortication is effective in the management of ADPKD. This approach is indicated primarily for renal pain due to cyst enlargement. The procedure has also been found to assist with control of hypertension. This surgery should aim to achieve decortication of all cysts that are accessible without caliceal violation.

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## Caliceal diverticula and infundibular stenosis

Debora K Moore and John C Hulbert

### CALICEAL DIVERTICULA

According to Prather the first description of what was probably a caliceal diverticulum was made in 1841 by Rayer, who referred to the structure as *kystes urinaires*.<sup>1,2</sup> Other terms include partial hydronephrosis, hydrocalicosis, pyogenic cyst, or caliceal diverticulum<sup>3-7</sup> (Figure 17.1).

A caliceal diverticulum is a cystic urine-containing cavity within the renal parenchyma, which is lined by nonsecretory, transitional epithelium and communicates with the renal pelvis or a calyx through a narrow channel. The diverticulum cavity fills with urine via a passive process and drains poorly. Caliceal diverticula have been estimated to occur in 0.21–0.45% of intravenous pyelograms (IVPs).<sup>8-11</sup> The majority of diverticula are asymptomatic but occasionally contain stones or cause recurrent urinary tract infections. Calculi occur within the caliceal diverticulum in 9.5–39%<sup>8,9,12</sup>—Yow and Bunts predicted as many as 50% contain calculi<sup>13</sup>—of cases and it is unusual for them to pass spontaneously because of the narrow caliber of the diverticular opening. Obstruction of the channel may be associated with severe pain and may lead to sepsis, spontaneous rupture, abscess formation, xanthogranulomatous pyelonephritis, kidney rupture, or even hypertension, proving that despite having a benign



**Figure 17.1** CT scan of a caliceal diverticulum: an eventration of the upper collecting system that lies within the renal parenchyma and communicates with the main collecting system through a narrow neck.

radiographic finding, caliceal diverticula do not always have benign outcomes.<sup>14–18</sup>

### **Etiology and embryology**

Several proposals have been offered as to the pathogenesis of the pyelocaliceal diverticulum, including

1. it is a residual of the rupture of a simple serous cyst into the collecting system
2. it arises by the progressive dilatation of a calyx in which the neck does not relax (achalasia) to allow proper drainage
3. it is the result of a fibrous infundibular stenosis secondary to stone formation in the calix.

In 1935 Quinby and Bright proposed that pyelogenic cysts originate from an aberration of the development of the renal pelvis in embryo.<sup>19</sup> In 1953 Wygrens stated that these cysts were probably congenital.<sup>20</sup> In 1967 Rosenberg suggested that they resulted as a developmental defect of the Wolffian ducts.<sup>21</sup> Most sources believe that caliceal diverticula are congenital structures rather than acquired ones.

### Differential diagnosis

Caliceal diverticulum seldom presents a diagnostic problem. Typically, a round or oval smooth-walled cavity is demonstrated in or around the corticomedullary junction and is seen as the only abnormality in an otherwise normal kidney and pyelocaliceal system. The size of such a cavity varies from 0.5 to 7.5 cm.<sup>22</sup>

Larger communicating cavities, especially those that tend to the cortical margin, should raise the possibility of a ruptured simple traumatic or spontaneous serous cyst rather than a simple caliceal diverticulum. In the absence of a previous examination demonstrating a serous cyst, the nature of a communicating cavity can only be determined by histologic analysis of the lining membrane with a serous cyst demonstrating flattened cuboidal epithelium. The diverticulum should not be confused with a hydrocalix, the diagnosis of which should be reserved for cases with caliceal obstruction caused by infundibular stenosis or stone obstruction. Other occasional differentials include microcalix, old papillary necrosis, tuberculosis, and an excavating abscess cavity of hematogenous origin. Caliceal diverticula are usually solitary, larger than the cystic dilatations of medullary sponge kidney, and project into the cortex rather than into the medulla. The diagnosis of caliceal diverticulum is established by demonstrating a narrow neck leading from a caliceal fornix to the diverticular pouch. Diverticula are found in both sexes and not infrequently contain stones (36% in one large series).<sup>23</sup> Diverticula can be found in children. Analysis of the diverticular calculi show that they are usually calcium oxalate, calcium phosphate, or carbonate apatite. Calculi may be single and as large as the diverticulum itself or multiple and small. In the latter instance, clustered calculi each 1–2 mm in diameter are referred to as 'seed' calculi. Concretations even smaller than seed calculi are commonly seen in caliceal diverticula and are referred to as 'milk of calcium.' The diverticulum with multiple opaque stones in the right kidney may simulate gallstones on a plain film of the abdomen.

### Indications for treatment

Indications for a procedure include chronic or recurrent pain referable to the diverticulum, recurrent or intractable urinary tract infection, radiographic evidence of progressive renal damage in the area of the diverticulum, or occupational reasons, as in the airline industry. In the absence of these findings periodic outpatient follow-up has been suggested. To date, there are no reports on the rate of progression of asymptomatic caliceal diverticula to symptomatic in these followed patients.

### Treatment options

Prior to treatment one must establish the relationship of the diverticulum to the calices. Is the location of the diverticulum anterior or posterior? Are there multiple stones or only a single stone? In addition to a standard IVP or retrograde pyelogram to delineate the intrarenal anatomy, a computed tomography (CT) scan may be necessary to evaluate the spatial relations of the stone within the kidney and to the surrounding structures.

Once the location of the diverticulum and stone burden is known, the approach as well as the best treatment option can be planned. Therapeutic alternatives available for patients with symptomatic caliceal diverticula are open surgery, shock wave lithotripsy (SWL), ureteroscopy, the percutaneous approach, or laparoscopic surgery.

### *Open surgery*

Traditional open surgery for the management of symptomatic caliceal diverticula consists of excision of the outer dome of the diverticulum followed by marsupialization of the edges with interrupted 3–0 SAS sutures. Once identified, the diverticular neck is obliterated. Obliteration can be via circumferentially incising it and inverting the wall with 3–0 SAS sutures or the opening can be fulgurated. (If needed, diluted methylene blue may be injected into the renal pelvis to identify the neck of the diverticulum.) The operative cavity may be packed with perinephric fat and a drain is positioned adjacent to the kidney. In the post-operative period, prolonged urinary drainage indicates incomplete closure of the diverticular neck and other post-operative complications are similar to those after a partial nephrectomy.<sup>24</sup>

In the past, some investigators have performed a partial or even total nephrectomy for deeper, larger, or polar diverticula. Today, open surgery for treatment of caliceal diverticulum is of historical value, as other minimally invasive options are available.

### *Shock wave lithotripsy*

In 1986 Wilbert et al reported that the use of SWL in 16 patients with caliceal diverticular stones rendered 20% of patients stone free at 3 month follow-up. They asked 'Is SWL worthwhile?'<sup>25</sup> Shortly thereafter, Psihramis and Dretler advocated SWL as the best treatment for stones in caliceal diverticula.<sup>26</sup> They described SWL as a safer modality with lower morbidity and acceptable treatment outcomes for symptoms when compared to the more invasive percutaneous approach. However, of the 10 patients they treated with SWL, only 2 successfully passed all the stone fragments and 3 (30%) had persistent symptoms after an average follow-up of 5.9 months. Furthermore, 30% of their patients required a second SWL for complete fragmentation of the stones. Jones et al reported similar ineffective results; they treated 40 caliceal diverticula in 39 patients. Of these patients only 26 were treated by SWL. These patients had a stone-free rate of 4% (1 in 26); 10 of the 26 (38.5%) patients required further treatment due to the persistence of symptoms.<sup>27</sup> Stroom and Yost—following the dictums for SWL use, or more specifically, that if obstruction below the calculus occurs, which is the case in most caliceal diverticula, SWL is relatively contraindicated—carefully selected for patients with stones <15 mm in diameter in caliceal diverticula with a proven radiographically patent diverticular neck. This approach achieved a stone-free rate of 58% (11 of 19 patients). In 86% of the 14 patients presenting with flank pain, symptoms completely resolved after treatment.<sup>28</sup> Ritchie et al and others had also noted symptomatic improvement in 75% of the patients treated with SWL, irrespective of stone-free results.<sup>26,29</sup>

Despite these reports with dramatic improvement in symptoms and stone-free rates from 4 to 58%, SWL as a primary treatment modality for caliceal diverticula with calculi remains controversial (Table 17.1). A main concern

**Table 17.1** *Primary SWS (shock wave lithotripsy) treatment of caliceal diverticular stones*

| Investigator                        | No. of stonefilled tics | Stone size (mm) | Diverticulum location (pole) | Stone-free rate | Further treatment (N) | Symptom-free at follow-up | Follow-up time (months) |
|-------------------------------------|-------------------------|-----------------|------------------------------|-----------------|-----------------------|---------------------------|-------------------------|
| Wilbert et al <sup>25</sup>         | 16                      | 4–25            | NA                           | 20%             | NA                    | NA                        | 3                       |
| Psihramis and Dretler <sup>26</sup> | 10                      | 0.9–14          | Upper–7                      | 14% (1/7)       | 2                     | 57% (4/7)                 | 4.9 mean, range 3–7     |
|                                     |                         |                 | Mid–2                        | 50% (1/2)       | 1                     | 100% (2/2)                | 7.5 mean                |
|                                     |                         |                 | Lower–1                      | 0%              | 0                     | 100% (1/1)                | 10                      |
| Jones et al <sup>27</sup>           | 26                      | NA              | Upper–9                      | 4% (1/26)       | 2                     | 36% (9/26) <sup>a</sup>   | 35 mean                 |
|                                     |                         |                 | Mid–9                        | 0%              | 4                     |                           |                         |
|                                     |                         |                 | Lower–8                      | 0%              | 4                     |                           |                         |
| Streem and Yost <sup>28</sup>       | 21                      | 3–15 (mean 7.9) | Upper–11                     | 64% (7/11)      | NA                    | 86% <sup>b</sup>          | 1                       |
|                                     |                         |                 | Mid–3                        | 33% (1/3)       | NA                    |                           |                         |
|                                     |                         |                 | Lower–7                      | 57% (4/7)       | NA                    |                           |                         |

NA=not available. <sup>a</sup>Not specified by location, overall rate. <sup>b</sup>Overall rate, not by location and symptoms resolved despite residual stone; however, a stone-free state was always related to a symptom-free state

has been the belief that the diverticulum itself is the primary abnormality, and that an obstructed or relatively narrow neck leads to urinary stasis and subsequently to stone formation. Therefore, even if a stone-free status could be achieved initially, treatment such as SWL, which addresses only the stone, might prove to be temporizing rather than definitive, although long-term results of this approach are unknown. In contrast, operative intervention and percutaneous techniques, while clearly more invasive, have been designed not only to remove the stone but also to obliterate the diverticulum, or at least provide improved drainage.<sup>11</sup>

Streem et al also bring up the concept that stone formation in caliceal diverticula is primarily a result of localized obstruction, and stasis is not necessarily relevant in all cases. They argue that, since in select cases, a relatively high stone-free rate can be achieved with SWL alone, this suggests that an anatomically narrow diverticular neck is not necessarily a physiologically obstructing lesion. Furthermore, while most caliceal diverticula are considered congenital in origin, at least some are thought to be acquired lesions resulting from localized inflammation associated with infection or primary calculus disease.<sup>8,30</sup> They suggest the concept that some diverticula are in fact acquired lesions is particularly relevant in patients whose diverticula are associated with stones in most series if one notes the incidence of coexisting stone disease unrelated to that in the diverticulum of up to 40%.<sup>9,26,28</sup>

Treatment of caliceal diverticula with stones via SWL may provide temporary relief of symptoms but it does not address the diverticulum itself. Therefore, a trial of shock wave lithotripsy is justified:

1. for diverticula containing stones 1 cm or less and a functionally patent neck (contrast drains from diverticulum in delayed films during IVP)
2. in centers with little experience in more definitive procedures (percutaneous, ureteroscopy, laparoscopic)
3. in patients adamantly opposed to invasive procedures.

### *Ureteroscopy*

First reported in 1989 by Fuchs and David, ureteroscopy for the management of symptomatic caliceal diverticulum with and without SWL achieved a stone-free rate of 73%, can provide effective symptom-free results.<sup>31</sup> Their results and 86% of the patients had resolution of their symptoms. In 1992, Pang et al reported on 36 patients with symptomatic caliceal diverticula stones. If one accounts for only upper and mid-renal calculi, then 75% (24 out of 32) were rendered stone-free; if one looks at all patients regardless of location of diverticula, then approximately 67% were rendered stone free by ureteroscopy.<sup>32</sup> Another series had an overall success rate of 84% (16 of 19) for upper- and mid-pole diverticula and a 29% (2 of 7) success rate for lower-pole diverticula in entering and dilating or incising the neck of the diverticulum. In this series, of the 18 diverticula successfully entered using a retrograde approach, only 15 (83%) were rendered stone free. The authors' goal was to render the patients stone and symptom free and the overall diverticular obliteration rate was not reported.<sup>33</sup> Auge et al retrospectively compared percutaneous nephrolithotripsy (PCNL) and ureteroscopy for the management of symptomatic caliceal diverticula.<sup>34</sup> Fifty six percent (22 of 39) of patients underwent PCNL and 44% (17 of 39) were managed by ureteroscopy. All ureteroscopy cases were performed as outpatient procedures while the mean hospital stay for the PCNL group was 2.8 days. Nineteen percent of the ureteroscopy group was stone free on follow-up IVP vs 78% of those undergoing PCNL. No complications occurred in the ureteroscopy group while 4 patients had complications in the PCNL group, including pneumothorax and pneumohemothorax. Thirty five percent (6 of 17) of the ureteroscopy group were symptom free at 6 week follow-up, yet 86% of the PCNL group were completely symptom free at 6 week follow-up.

Next, in a study done by Moore et al, a comparison of SWL, ureteroscopy, PCNL, and the laparoscopic approach in treating caliceal diverticula revealed that only 50% of the patients treated by ureteroscopy alone had successful treatment of symptoms. The 2 patients that failed underwent subsequent laparoscopic treatment with 100% obliteration, 100% symptom free rate, and no complications.<sup>35</sup>

Ureteroscopy for the treatment of caliceal diverticula with stones is an attractive initial option for small diverticula limited to upper or middle caliceal diverticula with a small stone burden (less than 1 cm) and a short accessible, diverticular neck.<sup>36</sup> Stone-free rates range from 36 to 84% for upper- and mid-pole stone-filled caliceal diverticula. Lower-pole stone-free rates, as one would expect, are much lower and range from 0 to 29% (Table 17.2). Indications for ureteroscopic treatment of caliceal diverticula with calculi



are similar to SWL. To date, no attempts using prone ureteroscopy have been reported to aid in ureteroscopically accessing the diverticulum located in the lower pole.

### *Percutaneous renal surgery*

Since 1984, when Reddy and coworkers reported on its successful use, percutaneous nephrolithotomy has been the treatment of choice for symptomatic stones in caliceal diverticula.<sup>37</sup> Subsequent reports have confirmed the efficacy of this approach, with recent stone clearance rates from 80% to 100%.<sup>27,38–46</sup> The procedure, albeit successful, is complex and requires a high degree of technical

**Table 17.2** *Ureteroscopy as primary treatment of caliceal diverticular stones*

| Investigator                     | No. of stone-filled tics | Diverticulum location (pole) | Stone-free rate     |
|----------------------------------|--------------------------|------------------------------|---------------------|
| Pang et al <sup>32</sup>         | 36                       | Upper/mid—32                 | 75% (24/32)         |
|                                  |                          | Lower—4                      | 0% (0/4)            |
|                                  |                          |                              | Overall 67% (24/36) |
| Batter and Dretler <sup>33</sup> | 26                       | Upper/mid—19                 | 84% (16/19)         |
|                                  |                          | Lower—7                      | 29% (2/7)           |
|                                  |                          |                              | Overall 69% (18/26) |
| Auge et al <sup>34</sup>         | 17                       | Upper—11                     | 36% (4/11)          |
|                                  |                          | Mid—4                        | 0% (0/4)            |
|                                  |                          | Lower—2                      | 0% (0/2)            |
|                                  |                          |                              | Overall 24% (4/17)  |
| Moore et al <sup>35</sup>        |                          | Upper/mid—4                  | 50% (2/4)           |
|                                  |                          |                              | Overall 50% (2/4)   |

expertise. Complications such as bleeding and sepsis are associated with the procedure.

### **Direct vs indirect puncture of the diverticulum**

In 1986 Hulbert et al described 10 patients with 11 calculus containing caliceal diverticula.<sup>11</sup> In 8 cases, the diverticulum was punctured directly, while in the remaining 3 cases the diverticula were approached indirectly through another calyx. When the calyx was punctured directly, the nephrostomy tract was dilated and the calculi removed. The diverticular neck was then dilated and a large nephrostomy tube placed across the neck into the collecting system. In the 3 cases using the indirect approach, the neck was dilated ( $n=1$ ) or incised ( $n=2$ ) and the calculus removed. No treatment was given to any diverticulum, as the authors believed that after 2 weeks the traumatized diverticular lining becomes obliterated by granulation around the tube. On follow-up, the diverticulum treated with an indirect puncture failed to be obliterated, suggesting that direct puncture of a diverticulum is important. Other investigators have supported the fact that direct access is required to provide the best opportunity to remove the stones and treat the diverticulum.<sup>27,39–41</sup>

### Fulguration of the diverticular wall vs no fulguration

In 1984 Clayman et al reported on fulguration of bladder diverticula with relief of obstruction. Rapid resolution of the diverticula resulted. In their earlier report the authors felt that 'unlike bladder diverticulum a caliceal diverticulum is attached to firm renal parenchyma, which may prevent shrinkage in some cases'.<sup>47</sup>

Currently, Hulbert et al fulgurates the diverticular wall only when the diverticulum is >2.0 cm. His obliteration rate is roughly 83.3%.<sup>48</sup> Jones et al fulgurated all the diverticulum walls in 24 procedures and had 100% obliteration of the diverticulum.<sup>27</sup> Bellman et al fulgurated the diverticular wall in 20 procedures and reported 80% obliteration.<sup>44</sup> Shalhav et al reported fulguration of the wall in 14 procedures, which resulted in 86 % (12/14) successful obliteration and only 50% (3/6) successful obliteration in those not fulgurated.<sup>41</sup> Recently, Landry et al could not fulgurate the diverticulum in 7 cases because of anterior location or 'preoperative local hemorrhage' and they had 35% of patients (11/31) that on IVP follow-up had persistence of a diverticulum. Upon review of these failures, 63.6% (7/11) were also found not to have had the diverticular neck dilated.<sup>45</sup>

### Treatment options for the diverticular neck

**Incision.** Shalhav et al reported 83% (10/12 cases) successful obliteration when the diverticular neck was incised.<sup>41</sup> While Landry et al with fulguration of the diverticulum wall and incision of the diverticular neck demonstrated complete obliteration of the diverticula on follow up only 66.7% (20/31) and 88% of these patients were asymptomatic. It was also discovered that ~45% (5 of the 11) with persistent diverticulum had recurrent stones.<sup>45</sup>

**Dilation.** Jones et al, in their 24 cases, dilated the neck and fulgurated the diverticular wall with 100% obliteration and symptom-free status.<sup>27</sup> Bellman et al reported that, with dilation of the neck and fulguration of the wall in 20 cases, they had 80% obliteration rate and 100% symptomfree rate.<sup>44</sup> Shalhav et al had less success when dilating the diverticular neck, achieving only a 66% success rate.<sup>41</sup>

**No Treatment.** Monga et al recently reported on their unique approach in which they made no attempt to traverse the infundibulum. The investigators believe that it is 'intuitive' that if the goal is to collapse the cavity dilation or stenting is counterproductive.<sup>42</sup> In this study a total of 14 patients were treated. Mean diverticular diameter was 10.9 mm. All 14 became stone free, 100% demonstrated diverticular obliteration by CT examination, and there was one major complication. Mean follow-up in this population was 38 months (range 8–74).

Currently, the best approach for the percutaneous treatment of caliceal diverticulum has not been delineated. As previously demonstrated, in the hands of the experienced endourologist, multiple approaches have been successful. Currently, most endourologists advocate a direct puncture with incision of the neck and fulguration of the diverticular wall when possible. Summarizing the world literature, fulguration will cause ablation of 65–100% of lesions, including very large diverticula.<sup>11,20,35,38,42,45</sup> However, one should keep in mind that diverticula with diameters greater than 5 cm had the poorest outcome.

Overall, percutaneous management of caliceal diverticula is appropriate for the vast majority of cases, has a high success rate, and allows simultaneous elimination of the

primary anatomic abnormality (the diverticulum) as well as the source of symptoms (the calculus). Regardless of the size of the caliceal diverticula, they are amenable to percutaneous treatment of stone burden, diverticular size, or location, most symptomatic treatment.

Long-term follow-up in these patients to get an accurate measure of success appears to be greater than 12 months. Use of CT scan seems to be the most accurate means of establishing the absence or presence of a diverticulum post treatment.

**Technique.** Chapter 29 describes in great detail the necessary equipment and techniques needed for PCNL in caliceal diverticulum.

### *Laparoscopic ablation of caliceal diverticulum*

In 1993, Gluckman and associates performed the first laparoscopic ablation of a caliceal diverticulum with success.<sup>49</sup> In the same year, Winfield et al, using a more dramatic but still minimally invasive approach, reported the first laparoscopic partial nephrectomy for treatment of a lower-pole caliceal diverticulum containing a stone.<sup>50</sup> Again, in 1994 Ruckle and Segura used a laparoscopic approach to treat a symptomatic stone-filled, caliceal diverticulum with success and without complications.<sup>51</sup> Today, 32 cases on laparoscopic treatment of caliceal diverticula have been recorded. Review of this literature on using the laparoscopic approach in selected patients gives a 100% stone-free rate, a > 96% symptom-free rate, and >94% obliteration.<sup>48,51-58</sup>

Recently, Moore et al examined their results on treating caliceal diverticula with SWL, ureteroscopy, PCNL, or laparoscopically. Only a laparoscopic approach gave a 100% success rate for obliteration and removal of the stones without complications. They also found that the cost of laparoscopic vs PCNL was not statistically significant but postoperative pain, medication, and return to normal activity did show an advantage in the laparoscopically managed patients.<sup>35</sup>

### **Patient preparation**

Patient preparation mimics other urologic procedures. The urinary tract should be clear from infection. Use of a bowel preparation is dependent on surgeon preference, past surgical history, and surgical approach; i.e. if a retroperitoneal approach is used it is usually unnecessary. A broad-spectrum intravenous (IV) antibiotic is usually given at the beginning of the procedure and postoperative use is dependent on culture information and surgeon practice.

### **Localization of the diverticulum intraoperatively**

Key to successful treatment is localization of the diverticulum. The diverticulum can appear as a raised lobular area or a pit in the capsule. But, inflammation of the diverticulum from the calculi or infection may occur; scarring of the kidney at this site is common, causing adherence of fat and fibrous tissue. This process may obscure the pit, which must be dissected out. Should difficulty be encountered in identifying the diverticulum, further measures are available. The site may be probed with a needle on a laparoscopic holder or gallbladder needle to 'feel' for the calculus.<sup>51</sup> Methylene blue may be injected via the ureteral catheter, and this may be visible through the thin renal cortex

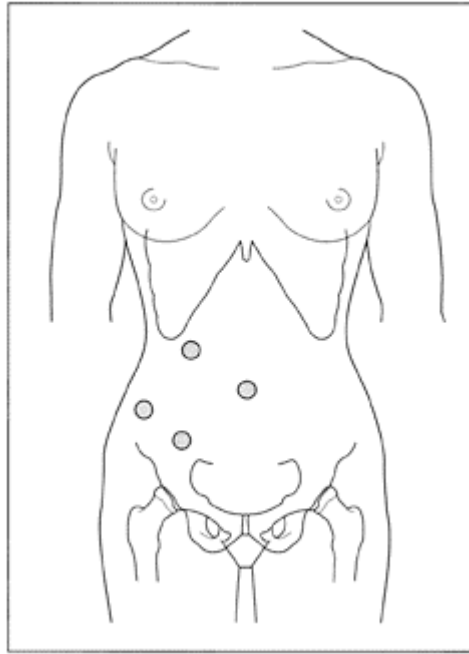
overlying the diverticulum or aspirated percutaneously with a long needle. Another option is use of fluoroscopy with a C-arm image intensifier to localize the stone, and contrast may be injected via the ureteral catheter to image the diverticulum. Lastly, laparoscopic ultrasonography is a safe and effective means of locating the calculi.<sup>53</sup> However, one needs to keep in mind that this imaging modality does have a learning curve and can be challenging if radiology is not available for interpretation of images at the beginning of the learning curve.

### Laparoscopic technique

At the start of the case a 6F or 7F external ureteral stent is placed in the renal pelvis. This will aid in identification of the proximal ureter and allow for injection of methylene blue or contrast. Depending on the location of the diverticulum as identified radiographically preoperatively and the surgeon's preference, a transperitoneal vs an extraperitoneal approach is planned. Both approaches are modified versions of a laparoscopic simple nephrectomy and for more details Chapter 34 should be reviewed.

**Transperitoneal approach.** Port placement varies with operator experience and preference. Commonly, the more inexperienced surgeon will use more sites and larger ports. As the surgeon develops his technique, modifications are made. The following figures are guides and are not to be taken as the only approach but as a starting point. The patient may be positioned in the flank or modified flank position. Although 5 ports have been traditionally used for laparoscopic nephrectomy, most surgeons use 4 ports when performing laparoscopic caliceal diverticula ablation, with the option of adding another port if liver or spleen retraction is needed. Examples of port placement can be seen in Figure 17.2. The laparoscopic ports are placed in various combinations to give the surgeon the best access for dissection, and trocar placement is dictated by diverticulum location.

Following port placement, for right-sided cases, the right colon is mobilized along the white line of Toldt using grasping forceps and the electrocautery scissors. The colon is reflected medially, and the retroperitoneum visualized. For left-sided cases, the lienorenal and phrenicocolic ligaments may need to be coagulated and incised or clipped, depending on their size. This enables one to move the spleen medially away from the kidney. The peritoneal incision is carried out medially so that the left colon can be moved medially, thereby exposing Gerota's fascia. Once Gerota's fascia is identified, using grasping forceps and scissors, it is incised and dissected from the kidney. The caliceal diverticulum is identified by one of the techniques previously discussed, incised, and the roof removed. The calculi if present are visualized and removed using spoon graspers or irrigation and suction. The entire cavity, including the connection with the collecting system, is fulgurated with electrocautery or the argon beam coagulator, and the diverticulum is marsupialized. Methylene blue, injected via the ureteral catheter, can be used to reveal the communication to the collecting system: once identified, the communicating track is fulgurated. The neck of the diverticulum can also be closed with conventional laparoscopic suturing with 2-0 PDS on a CT-1 needle over a surgical bolster. This can be tedious and some believe not necessary.<sup>56,59</sup> Reinjection of methylene blue is a good check system to verify lack of further communication.



**Figure 17.2** Laparoscopic port placement will be dependent on patient body habitus and surgeon experience/preference but general guidelines are as follows for a transperitoneal approach. Four ports are placed in the following locations: inferior umbilical incision for the camera; midway between the anterosuperior iliac spine and umbilicus; subcostally in the anterior axillary line; and, subcostally in the midclavicular line.

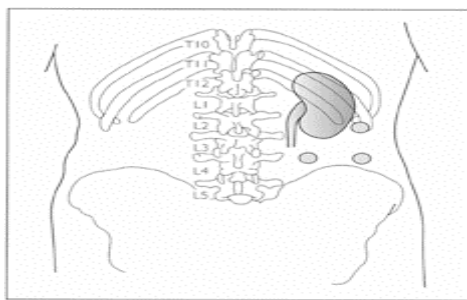
Alternatively, the diverticular defect can be obliterated by placing Gerota's fascia or fat into the defect with the aid of staples or suture. Others advocate the use of synthetic glue to save time and avoid suturing, which can be difficult for some.<sup>56</sup> One group left the defect open in 1 of 3 cases. The only partial obliteration of the diverticulum was in the system not closed, and therefore they suggested that the defect be closed for the best chance of obliterating the diverticulum.<sup>54</sup> Moore et al advocate the sutured closure of the caliceal diverticulum with 2-0 PDS in a running imbricated fashion with woven Surgicel

and fibrin glue to fill the base of the diverticular defect. To date, there have been no failures in the patients treated in this manner.<sup>52</sup> A drain is placed through a laparoscopic port adjacent to the area and all remaining ports are removed under direct vision.

**Extraperitoneal approach.** A ureteral catheter is placed cystoscopically. The patient is then placed in the full flank position or lateral decubitus, and a 2 cm incision is made over the lumbar triangle, lateral to the erector spinae muscle, and just above the iliac crest. The incision is deepened by blunt dissection to the fascia overlying the lumbar triangle, which is sharply incised. A finger is pushed through between the bundles of the internal oblique and transversus muscles into the retroperitoneal space. Using blunt finger dissection the peritoneal reflection is gently pushed as far medially as possible and the lower pole of the kidney is palpated. A balloon dilator is inflated outside Gerota's fascia, and the ports are placed (Figure 17.3). Gerota's fascia is identified and incised and the kidney is mobilized. For lower-pole diverticulum the ureter is found by incising Gerota's fascia as far posteriorly as possible, parallel with the psoas muscle. After identification of the diverticulum, the procedure is performed as in the transperitoneal approach.

The extraperitoneal approach provides good access to the kidney without breach of the peritoneum, minimizing problems should there be a urine leak postoperatively. It also avoids the potential problems of transperitoneal access: namely, hazards associated with establishing a pneumoperitoneum bowel injury, bleeding from vessel injury, and hernia formation. Disadvantages include a smaller working space, making conventional suturing difficult, and unfamiliar landmarks. Some will use the retroperitoneal approach initially and, as the case progresses, if need be to open up the peritoneum.

The bottom line is that the retroperitoneal approach offers the patients the advantages of monotherapy, a low risk of morbidity, and an excellent opportunity for resolution of the symptoms.<sup>54</sup> However, complete diverticular ablation via conventional laparoscopic suturing may not be possible secondary to the small 'working space', potentially increasing the failure rate.



**Figure 17.3** Laparoscopic port placement for extraperitoneal approach. An initial port is placed over the lumbar triangle, lateral to the erector spinae muscle and just above the iliac crest; 2–3 other ports are

placed, consisting of a 12 mm, 10 mm,  
and a 5 mm port, as necessary.

**Troubleshooting.** An upper-pole diverticulum may be difficult to access because of the inability to position trocars over the upper-pole diverticulum secondary to the rib cage. Difficulty with access can be lessened by a flexible-tip laparoscopic camera, placing trocars just off the ribs, and completely mobilizing the kidney within Gerota's fascia. After mobilization of the renal unit, the kidney can be retracted downward to give better access to the diverticulum.

Overall, laparoscopic caliceal diverticulectomy has the potential to provide an effective means of complete removal of all calculi and permanent obliteration of the diverticulum with the least amount of patient morbidity. In specific cases, such as an anterior upper-pole location or failed previous procedure, this is the procedure of choice.

### **Treatment of pediatric caliceal diverticula**

Fifteen cases of pediatric caliceal diverticula have been reported in the world literature to date.<sup>15,60,61</sup> Like their adult counterparts, prior to endourological advancements, open surgical treatment options were the mainstay for pediatric treatment.<sup>15,60</sup>

In 1999, Hulbert et al first reported on their series of percutaneous treatment of caliceal diverticulum in the pediatric population.<sup>61</sup> In their series one patient had failed SWL but was successfully treated by PCNL. When compared to adults treated in the same fashion the children did equally as well if not better (Table 17.3).<sup>48</sup> Longterm follow-up of these pediatric patients revealed 100% success rate for symptoms, treatment of the stone, and obliteration of the diverticulum.<sup>62</sup>

Pediatric patients with symptomatic caliceal diverticulum have been treated via open surgery, SWL, and PCNL according to the literature. Currently, PCNL has proven to be efficacious and the least invasive.

### **Conclusion**

Every patient deserves assessment of their unique scenario and the treatment option pursued needs to be based on sound principles. Knowing the literature, with results, complications, and shortcomings of each approach to caliceal diverticulum ablation, should better enable one to make a knowledge-based decision on the best approach for each individual patient. Whatever approach is used, all modalities of therapy need to provide safe and effective treatment of the problem with minimal loss of functional renal tissue.

### **INFUNDIBULAR STENOSIS**

Infundibular stenosis is rare and may be congenital or acquired. Infundibular stenosis is differentiated from a caliceal diverticulum by the presence of collecting tubules

**Table 17.3** *Results of percutaneous treatment of caliceal diverticula: adult vs pediatric*<sup>48</sup>

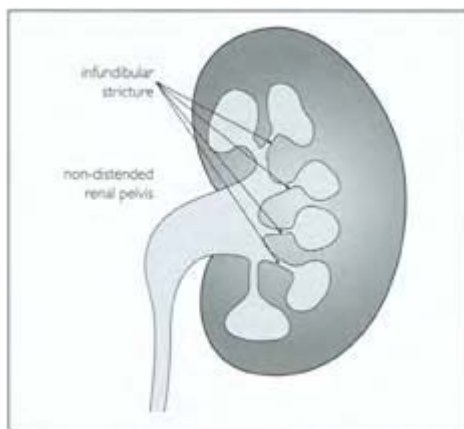
|   | Adult (n=20) | Pediatric (n=4) |
|---|--------------|-----------------|
| Length of procedure (min):                |              |                 |
| Mean                                      | 142.5 (n=15) | 57.3 (n=3)      |
| Range                                     | 45–320       | 33–84           |
| Successful stone removal on first attempt | No           | Yes             |
| Successful obliteration of diverticulum   | 16/20 (80%)  | 4/4 (100%)      |
| Complications                             | Yes          | No              |

within the dilated calyx: recall that a caliceal diverticulum is lined by transitional epithelium.<sup>63</sup> Radiographically, regardless of type, infundibular stenosis is a dilated calyx draining through a narrowed infundibulum into a nondistended renal pelvis (Figure 17.4). Patients with infundibular stenosis commonly present with pain.

### Congenital

The congenital abnormality was originally characterized by Kelalis and Malek in 1981.<sup>64</sup> It was initially defined as a relatively benign process in which ‘renal function remains stable and rarely deteriorates’.<sup>64, 65</sup> Infundibular obstruction or achalasia is due to the hypertrophy of the muscular layer of the infundibulum or alternatively to abnormal collagen deposition within the infundibular muscle layer. In a retrospective review, Husmann et al found that the renal function did not remain stable, as previously believed. They found that patients with infundibular stenosis were at risk for a hyperfiltration injury.<sup>66</sup> They suggest that after initial diagnosis a voiding cystourethrogram should be performed to evaluate for the presence of vesicoureteral reflux. If reflux is identified, appropriate management should be instated. A baseline serum creatinine and glomerular filtration rate (GFR) are useful. Follow-up should be indefinite and individualized. At a minimum, they suggest a physical examination, urinalysis, serum creatinine, GFR, and upper tract radiologic evaluation should be performed yearly. According to Husmann et al,





**Figure 17.4** Infundibular stenosis. Radiographically, infundibular stenosis is represented as a dilated calyx draining through a narrowed infundibulum into a nondistended renal pelvis.

for some patients with hypertension, proteinuria or basically presenting with advancing renal insufficiency, dietary restriction of protein and treatment of hypertension with calcium channel blocking agents or angiotensin-converting enzyme (ACE) inhibitors may be of some benefit in lessening the rapid decrease in renal function due to hyperfiltration injury. However, if evidence of obstruction or progressive hydronephrosis is identified, they recommend prompt operative intervention.

### Acquired infundibular stenosis

In the past, acquired intrarenal scarring was primarily associated with tuberculosis. Today, acquired infundibular stenosis is a rare clinical entity related to chronic inflammatory disease, recurrent, reflux-induced pyelonephritis or secondary to percutaneous nephrolithotomy.<sup>67-75</sup> Failure to institute surgical treatment invariably results in progressive dilatation of calices proximal to the stenotic lesion, hydronephrosis, and, if left untreated, segmental loss of renal parenchyma or eventually end-stage renal disease. Bodner et al treated 3 patients in whom infundibular stenosis was caused by ileal-ureteral reflux and chronic urinary infection with observation alone. All 3 patients experienced progressive renal deterioration.<sup>75</sup>

The endoscopic treatment of infundibular stenosis is similar to the treatment of a symptomatic caliceal diverticulum: more specifically, percutaneous endoscopy or retrograde ureteroscopy. Ureteroscopy with cold knife incision and laser ablation have been successfully performed for tubercular as well as congenital stenosis.<sup>76,77</sup>

Review of the world literature reveals 12 cases of reported acquired stenosis after PCNL.<sup>69–75</sup> Recently, Parsons et al looked at their rate of acquired stenosis after PCNL and found that 2% (5 of 223) developed this complication.<sup>74</sup> Stenosis appeared within 1 year of the initial PCNL and developed in areas corresponding to the previous sites of the PCNL access. The severity of narrowing was graded as mild, moderate, or severe and was based on the severity of the collecting system dilatation proximal to the obstruction. Therefore, in the 5 patients diagnosed with infundibular stenosis post PCNL, they regarded 4 as mild to moderate. These patients were managed by observation or endoscopic dilation. The single patient with severe stenosis was found to have renal impairment. Review of their perioperative, operative, and postoperative data revealed an association of infundibular stenosis following PCNL with prolonged operative time (mean time of 258 min), a large stone burden requiring multiple removal procedures, and extended postoperative nephrostomy tube drainage (mean time of 33 days with range of 2–24).

## Treatment

### *Endoscopic infundibulotomy*

Prior to the advent of minimally invasive techniques, calyorrhaphy, ileocalycostomy, and other types of upper urinary tract reconstruction to relieve infundibular obstruction were commonly employed for the treatment of infundibular stenosis. Treatment with a partial nephrectomy or even total nephrectomy was not uncommon when tuberculosis was the origin of the infundibular stenosis.<sup>78–81</sup> With technological advances, open procedures are no longer the first line of treatment options in most situations.

### *Antegrade approach*

Some investigators recommend a retrograde study prior to manipulation to better judge if the stenotic area can be transversed and allow planning of an appropriate approach, antegrade vs retrograde. If an antegrade approach is reasonable, a percutaneous nephrostomy is made into the dilated calyx and the tract dilated followed by placement of a working sheath. A retrograde ureteral catheter is placed prior to the start of the procedure. A guide wire is maneuvered through the stricture with the injection of indigo carmine through the retrograde catheter. If the guide wire cannot be passed in such a fashion, one may use a 10F ureteroscope to traverse the stricture in an antegrade fashion. The stricture is dilated as large as possible up to a 20F using facial dilators or a balloon catheter over a guide wire. A second guide wire is inserted and an incision is made between the two guide wires on the lateral side. The incision is deepened until whitish fibrous scar tissue is separated. Any bleeding that occurs may be controlled by compression with the Amplatz dilator for about 5 min. A 14F Cook endopyelotomy catheter or a 20F nephrostomy catheter is placed through the stricture for 6–8 weeks.<sup>77</sup>

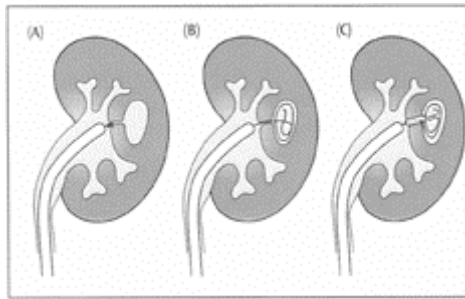
Notably, in 1992, Clayman and Kavoussi recommended incision along the mouth of the infundibulum in a radial fashion to avoid bleeding.<sup>82</sup> However, other investigators believe that this is not necessary, as a single incision appears to be sufficient in cases of

severe chronic inflammatory fibrous strictures.<sup>76,77</sup> Even if a single cut on the lateral side could cause some bleeding, it is usually easily controlled by compression with a balloon catheter or Amplatz dilator.<sup>76</sup>

*Retrograde approach: ureteroscopy and holmium:YAG (yttrium-aluminum-garnet) laser treatment*

With the refinement of ureteroscopes and the development of the holmium laser, several applications for its use have proven efficacious. Incisions with the holmium: YAG laser are very precise, with a soft tissue penetration less than 0.5 mm. Also, the 200  $\mu\text{m}$  fiber can be used through a flexible ureteroscope with continuous irrigation and minimal decrease in flexion; together, this allows precise control and control of the depth of the cut. Reviewing Kim and Gerber's experience with ureteroscopy with the use of the holmium:YAG laser, it appears to be a reasonable option in the treatment of select infundibular stenosis.<sup>77</sup>

To paraphrase their technique: a guide wire is introduced into the appropriate ureter and curled within the upper calyx. Next, a 10F double-lumen catheter is passed over the guide wire to dilate the ureter. In standard fashion, a safety guide wire is also placed. A 7.5F flexible ureteroscope is advanced over the wire and positioned in the renal pelvis. If the ureteroscope cannot be placed into the narrowed infundibulum, a 200  $\mu\text{m}$  holmium laser fiber is introduced through the ureteroscope. The infundibulum is widely incised in a single location, using a power setting of 1.2 J and 10 pulses/s. A retrograde pyelogram is performed and the narrowed area of question is evaluated. Next, a guide wire is placed into the recently opened calyx and the flexible ureteroscope removed. A 7 mm balloon dilator is



**Figure 17.5** Retrograde ureteroscopic approach to infundibular stenosis (A) When the ureteroscope cannot pass into the narrowed infundibulum, a 200  $\mu\text{m}$  holmium laser fiber is used to incise the infundibulum at a single location. Cut slowly, as the blood vessels around the infundibulum do

not follow a predictable path. (B) A guide wire is now easily passed through the infundibulum and coiled in the calyx. (C) A 7 mm balloon is passed over the guide wire and across the infundibulum and the infundibulum is dilated.

inserted over the guide wire and across the infundibulum. The balloon is inflated to 10 atm pressure and maintained for 5 min (Figure 17.5). The balloon catheter is removed and a 7F×26 cm double pigtail stent is placed and positioned with the proximal curl within the dilated, anterior midpole calyx. Gerber recommends removing the stent 4 weeks postoperatively and performs an IVP 6 weeks postoperatively. Gerber cautions that since vessels around the infundibulum do not follow a predictable path, one should cut slowly and allow the small vessels to be coagulated.<sup>77</sup>

### Conclusion

With the advancement of technology, open procedures are no longer the first line of treatment options for infundibular stenosis in most situations. Patients presenting with mild infundibular stenosis need follow-up with periodic ultrasound and serum creatinine measurement. In the patient with moderate stenosis, use of dilation and cold cut knife or laser ablation of scar tissue with close follow-up are effective. Lastly, patients with severe stenosis and significant impairment of the ipsilateral kidney require major surgery.<sup>66,74</sup> If the degree of involvement is unclear, appropriate radiographic studies are imperative to delineate renal function. More to the point, compulsive radiographic follow-up should be mainstay for those at risk for infundibular stenosis.

Whether acquired or congenital in origin, infundibular stenosis is a rare entity. Correct diagnosis with appropriate work-up along with laboratory and radiographic followup can prevent certain patients from having renal failure.

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## 18

# Upper urinary tract infection—medical, percutaneous and laparoscopic treatments

Volker Severin Lenk, Elias Hsu, John G Pattaras

Upper urinary tract infections (UTIs) in adult males are relatively rare. In contrast, adult females continue to have bacterial infections at an incidence ranging from 2% to 7%. In children during their first 6 years of life, 8% of all girls and 2% of all boys will have a symptomatic UTI.

The most frequent cause of upper UTI remains *Escherichia coli*. Other organisms are found in complicated infections, associated with diabetes mellitus, instrumentation, anatomic abnormalities, and immunosuppression. Long-term antibacterial therapy and/or immunosuppression often lead to fungal infection such as candidiasis.

A reappearance of tuberculosis is occurring, often with resistance to antituberculous drugs. In recent years, the incidence has increased in Europe by approximately onethird and in the United States by approximately 15%.

*Mycobacterium* (M.) *tuberculosis* remains the most frequent cause, but in immunosuppressed individuals, *M. bovis*, *M. avium-intracellulare*, and *M. kansasii* have also been reported.<sup>1</sup> Schistosomiasis ranks second behind malaria in the prevalence of human parasitic diseases. The chronic infection caused by *Schistosoma haematobium* may lead to severe pathologies, including inflammation, retention of urine, nephritis, ureteral obstruction, and hydronephrosis with subsequent renal insufficiency, and most seriously, the development of a bladder carcinoma. This disease affects as many as 200 million people, with the main areas of endemicity being developing countries in Africa and the Middle East.

## Bacterial infection

### Introduction

Bacterial urinary tract infections are among the most common infectious diseases. The majority of UTIs are caused by uropathogenic bacteria. Acute UTIs are associated with substantial morbidity, and this is made worse by the high likelihood of recurrent infections. Up to 25% of women who have a first UTI will have a second infection within 6 months.

Approximately 25% of women who have had an episode of acute cystitis developed recurrent UTIs. Cystitis has an incidence of 0.5–0.7 episodes per year among sexually



active women. In children during the first years of life, 8% of all girls and 2% of all boys will have a symptomatic UTI.<sup>2</sup> Uncomplicated UTIs in adult men are rare.

Patients with an upper tract UTI are generally more severely ill than patients with cystitis. The upper UTIs occur in both uncomplicated and complicated forms.

### *Pyelonephritis*

The most frequent cause of pyelonephritis and upper UTIs is *E. coli*, which is present in between 80 and 90% of UTIs and in up to 95% of acute pyelonephritis.<sup>3</sup> Other isolated gram-negative rods are *Proteus mirabilis* and *Klebsiella pneumoniae*. Within the gram-positive organisms, *Streptococcus agalactiae* and staphylococcus coagulans negative organisms are to be found.

Other organisms are detected in complicated infections associated with diabetes mellitus, instrumentation, stones, and immunosuppression.

### **Pathogenesis**

The pathogenesis of acute pyelonephritis is reviewed herein, with an emphasis on the virulence factors responsible for its initiation, including urothelial adhesion by P fimbriae of *E. coli* and other common factors including hemolysin and aerobactin.<sup>4</sup> Renal damage does not always ensue following such infection. It is seen when toxic oxygen radicals are released during the ischemic episode and the respiratory burst of phagocytosis is marked and prolonged. These events occur when effective antibacterial treatment is delayed, when the diagnosis is not established early, or when socioeconomic factors prevent treatment. The scarring of chronic pyelonephritis leads to the loss of renal tissue and function and may progress to end-stage renal disease.

### **Diagnosis**

Clinical symptoms in acute pyelonephritis include flank pain, fever, and urgency. Urine analysis (leukocytes, erythrocytes, bacteria) and cultures should be performed. Enzymatic screening tests (leukocytes, esterase dipstick, nitrite dipstick) have a low sensitivity for rapid bacteriuria screening.

Significant bacteriuria has been defined as finding more than  $10^5$  colony-forming units per milliliter of urine.

### **Therapy**

With effective antibacterial therapy, the immune response by both T and B lymphocytes leads to antibodies that assist in bacterial eradication. Therapy must be both rapid and effective.<sup>5</sup> In many instances, antibacterial agents may be used as outpatient therapy. If the Gram stain shows only gram-negative organisms and if the infection is community acquired, oral outpatient therapy with trimethoprim-sulfamethoxazole or a fluoroquinolone may suffice if the patient has no nausea. When the patient is septic, hospitalization and treatment with parenteral antibiotics are needed. Both ceftriaxone and gentamicin are cost-effective parenteral therapy because only once-daily dosing is

needed. If grampositive organisms are found, an enterococcus should be suspected, and a beta-lactam penicillin such as piperacillin or a third-generation cephalosporin such as ceftriaxone is indicated. If penicillin allergy exists, vancomycin should be used. If the patient does not improve rapidly, diagnostic studies including ultrasound and computed tomography (CT) will assist in the diagnosis of obstruction, abscess (Figure 18.1), or emphysematous pyelonephritis. Most of these complications are now rapidly treated by stent or percutaneous drainage, with surgical therapy following as needed. Complicated infections such as those occurring in patients with anatomic abnormalities, stone, or immunosuppression, are often caused by organisms other than *E. coli*, and long-term antibacterial therapy often leads to fungal infections such as candidiasis.

## Fungal infection

### *Introduction*

In the period 1980–1990, fungal infections comprised 7.9% (27,000 patients) of all infections reported to the National Nosocomial Infections Surveillance System.<sup>6</sup> Predisposing factors for invasive infection included chemotherapy, antibiotic therapy, human immunodeficiency virus (HIV) type infections, and organ transplantation.

Endemic (blastomycosis, coccidioidomycosis, histoplasmosis) and opportunistic fungi (aspergillosis, cryptococcosis, candidiasis) cause genitourinary infections that result in obstructive uropathy, fungemia, and death. After transplantation the most common fungal pathogens of the urinary tract are *Candida* and *Aspergillus*.<sup>7</sup>

### *Diagnosis*

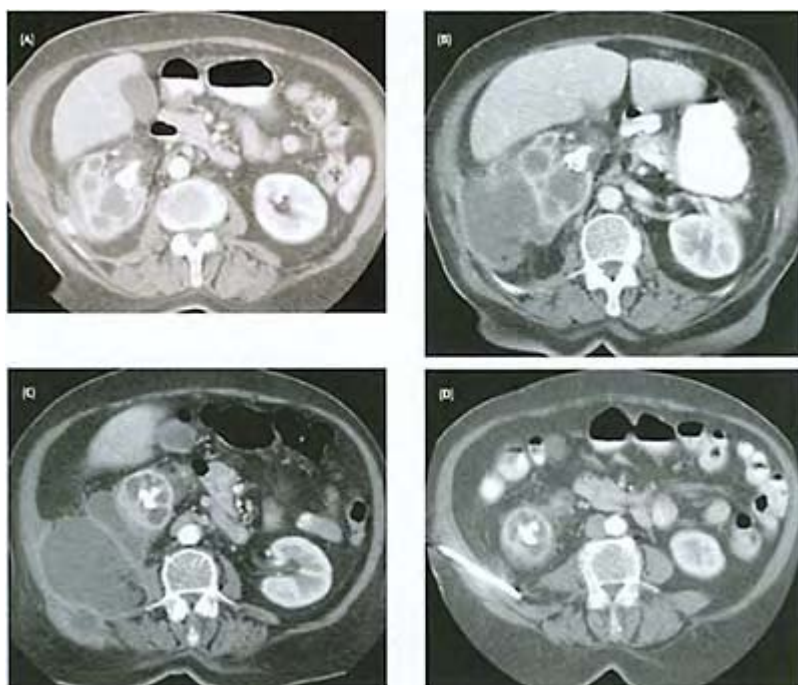
Often the primary diagnosis of fungal infection of the upper urinary tract is difficult. Culture or smear of urine, blood, or abscess material remain the standard methods of identifying the putative fungus. Colony counts > 15,000/ml (in the noncatheterized patient) will differentiate colonization from infection; however, the presence of indwelling catheters invalidates this method.

Numerous serology studies have been used, but none have provided adequate sensitivity or specificity to warrant clinical usage.

The development of the polymerase chain reaction (PCR) assay may provide a more rapid and sensitive laboratory tool with which to diagnose disseminated infection.

### *Therapy*

Although the azoles have been advocated for mild candidal urinary tract infection, the emergence of fluconazole-resistant *Candida albicans* gives credence to the continued use of amphotericin B bladder irrigations (50 mg/day for 7 days). The urologist must use knowledge, experience, and judgment in the evaluation and treatment of a patient with persistent candiduria. The algorithm (shown in Figure 18.2) provides a useful guide for the management of candiduria.<sup>8</sup>



**Figure 18.1**

Extensive paranephritic abscess on the basis of an infected hydronephrosis due to a staghorn calculus. Axial computer tomograms after intravenous application of contrast medium for the initial examination at the level of the renalis hilum (A), at the level of the lower third of the kidney (B), as well as after drainage of the abscess via pigtail catheter at the level of the renal hilum (C), and of the lower third of the kidney (D). In the initial examination (A and B) the typical picture of an extensive paranephritic abscess is to be seen. The kidney is dislocated in the medial direction by the abscess; in the medial third of the kidney the calices are enlarged because drainage is

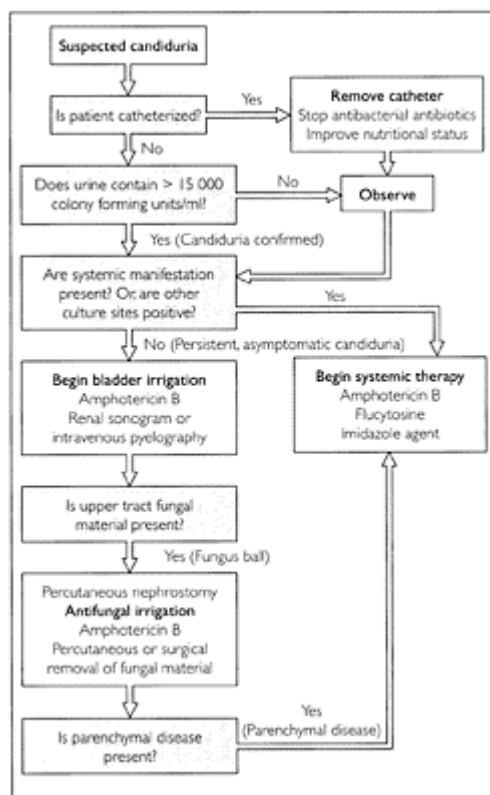
blocked by the staghorn calculus.  
Complete retrogression of the abscess  
after catheter drainage and picture of  
the draining catheter in place (C and  
D).

## **Parasitic infection**

### *Introduction*

Among the parasitic infections of the upper urinary tract only bilharziosis is of relevance. Schistosomiasis ranks second behind malaria in the prevalence of human parasitic diseases in the lower tract. Chronic infection caused by *Schistosoma haematobium*<sup>1</sup> may lead to severe disorders, including inflammation, retention of urine, nephritis, renal insufficiency (rarely) and, most seriously, the development of bladder carcinoma.

Praziquantel serves as an effective chemotherapy for schistosomiasis, killing the worms with high efficacy. However, given that the disease affects as many as 200 million people, with main areas of endemicity being developing countries in Africa and the Middle East, reliable and inexpensive diagnostic methods as well as careful observations of regional prevalence, therapeutic success, and resurgence are all important.



**Figure 18.2** Recommended algorithm for management of suspected candiduria.

### Diagnosis

Genitourinary schistosomiasis due to *S. haematobium* is a common infection in males and females in endemic areas. Hemospermia might be a symptom of male genital schistosomiasis. Feldmeier et al<sup>9</sup> discuss the value of hemospermia as a diagnostic tool in evaluating male genital schistosomiasis. Postmortem histopathologic studies have shown that in patients infected with *S. haematobium* the seminal vesicles and the prostate are as frequently affected by egg-induced lesions as the urinary bladder. Findings in returning travellers indicate that hemospermia is likely to occur in the early stage of the disease. However, hemospermia has never been reported in morbidity studies in areas where *S. haematobium* is endemic. We believe that hemospermia usually occurs unnoticed and can only be diagnosed in the context of specific medical examinations, and conclude that hemospermia does not provide useful diagnostic information in the tropics.

Campagne et al<sup>10</sup> considered the value of a questionnaire and of urine tests as diagnostic techniques for urinary schistosomiasis control on 5 consecutive days at three

primary schools in Niger. The efficacy of the questionnaire for the evaluation of morbidity was low. In particular, the children's responses concerning hematuria were not objective, and questions concerning dysuria were poorly understood. Overall, the screening sensitivity of urine filtration was low where the level of endemicity was moderate. The authors emphasize that repeated examination of urine had a strong effect on the epidemiology profile of urinary schistosomiasis.

Salah et al<sup>11</sup> examined schistosomiasis morbidity by means of ultrasonography for the first time in Yemen, and Useh and Ejezie<sup>12</sup> studied types of water contact and perception of the disease in Nigeria. They found that bathing, swimming, and fishing were the main activities leading to infection, and frequency of contacts was more important than duration of exposure.

Histopathologic data from postmortem studies revealed female genital schistosomiasis at frequencies of 7–100% for lesions in the lower reproductive tract and 2–83% for lesions in the upper reproductive tract. The specific vasculature of the small pelvis enables adult worms of *S. haematobium* to migrate and transfer eggs to the genital organs. Female genital schistosomiasis may be an important risk factor for the spread of sexually transmitted diseases, especially HIV in these endemic regions.

A novel diagnostic tool, eosinophil cationic protein (ECP), as a marker for detection of the extent of egginduced granulomatous inflammation of the urinary tract in areas endemic to *S. haematobium*, was more sensitive than the median urinary egg count and ultrasonographically detectable pathology.<sup>13</sup>

### Therapy

Praziquantel is the treatment of choice in *S. haematobium* infection. In a prospective study, Ofoezie<sup>14</sup> investigated the effects of praziquantel therapy on urinary schistosomiasis during a period of low transmission in patients in southwest Nigeria. After treatment of 102 patients with praziquantel (40 mg/kg body weight) 88.8% showed parasitologic cure and over 99% showed reduction in pretreatment egg load. Overall, reinfection at 3, 6, and 12 months post-treatment was 9.2, 18.4, and 36.9%, respectively. The author concluded that the strategy of giving treatment at a period of low transmission is preferable in terms of preventing resurgence.

In complicated UTI caused by ureteric strictures following bilharziosis, percutaneous nephrostomy or stenting is necessary.

In patients with ureteric strictures and ureterolithiasis caused by schistosomiasis, a successful outcome following extracorporeal shock wave lithotripsy (ESWL) was described.<sup>15</sup>

### Conclusion

Schistosomiasis should be evaluated in the differential diagnosis of hematuria and complicated upper UTI in obstructive disease of the urinary tract, especially in people coming from areas where it is endemic and in tourists who have visited those areas.

## Tuberculosis

### *Introduction*

Since Robert Koch's discovery of the acid-fast bacillus in 1882, intensive study of diagnosis and treatment modalities has taken place.

Currently, in most industrial countries the incidence of newly diagnosed cases of tuberculosis is decreasing each year, but the worldwide prevalence of tuberculosis has remained almost the same as it was at the beginning of the 20th century. More than 95% of patients diagnosed with tuberculosis are living in so-called Third World countries. In these countries, a dramatic increase in the incidence of tuberculosis has been observed, and it appears to be closely linked to infection with HIV. Patients with acquired immunodeficiency syndrome (AIDS) are at a high risk of developing secondary infections such as tuberculosis. Prospective real-time surveillance of tuberculosis in HIV patients is needed in order to detect case clustering and to improve control of tuberculosis.

Nearly 20% of patients with tuberculosis develop extrapulmonary manifestations. Involvement of the genitourinary system is seen in 4–8% of patients. Genitourinary tuberculosis (GUTB) is the most common extrapulmonary manifestation.<sup>16</sup>

### *Diagnosis*

The most important step in diagnosing GUTB is the patient's history. The knowledge of tuberculosis infection early in life either as a primary pulmonary manifestation or as an extrapulmonary manifestation gives an important clue in a large number of cases. One has to be aware that the latency between the pulmonary manifestation and GUTB is enormous. In some cases more than 30 years pass before GUTB becomes evident.

Voiding problems and chronic urgency are typical but nonspecific symptoms in urinary tuberculosis. In men, chronic epididymitis is the typical manifestation of tuberculosis (Figure 18.3).

Other symptoms that sometimes occur include back, flank, and suprapubic pain, hematuria, frequency, and nocturia. Renal colic is uncommon, occurring in fewer than 10% of patients, and constitutional symptoms such as fever, weight loss, and night sweats are also unusual. Only one-third of patients have an abnormal chest X-ray.

The diagnosis of tuberculosis of the urinary tract is based on the finding of pyuria in the absence of infection as judged by culture on routine media.

Radiologic imaging can be helpful in detecting GUTB. Characteristic signs on intravenous pyelogram and CT are useful in depicting GUTB. Radiologic manifestations of tuberculosis allow earlier diagnosis and the timely initiation of appropriate therapy, thereby reducing patient morbidity.

In early disease, it is often possible on intravenous urography to detect changes in a single calyx with evidence of parenchymal necrosis, and typically there is calcification on the plain film. In more advanced disease, urography



**Figure 18.3** Tuberculous epididymitis with fistulas on both sides.



**Figure 18.4** Plain film showing abnormal calices with intrarenal strictures, dilatation of the renal pelvis, and tuberculous dilatation of the ureter of the right kidney (*M. tuberculosis* was isolated from the urine).





**Figure 18.5** Plain film showing progressive bladder tuberculosis with vesicoureteral reflux on both sides.

will show caliceal distortion, ureteric strictures (Figure 18.4), and bladder fibrosis (Figure 18.5).

Ultrasound examination of the urinary tract may reveal renal caliceal dilation and more overt evidence of obstruction.

A positive skin test supports the diagnosis of tuberculosis, but a negative skin test does not necessarily exclude an extrapulmonary manifestation. This is especially true in cases of GUTB.

A microbiologic diagnosis of tuberculosis is usually made by isolation of the causative organism from urine or biopsy material on conventional solid media or by an automated system such as radiometry.

In recent years, nucleic acid amplification techniques, such as PCR, have been investigated extensively for the detection of *M. tuberculosis* and other mycobacteria in clinical specimens, notably sputum. Relatively few studies have specifically evaluated PCR for detection of GUTB, and these show the technique to be sensitive and specific, although some urine specimens contain inhibitory substances. In addition, PCR has been used to detect mycobacterial DNA in urine in cases of HIV-related disseminated tuberculosis.<sup>17</sup>

A positive culture or histologic analysis of biopsy specimens, possibly combined with PCR, is still required in most patients for a definitive diagnosis. In 25–30% the diagnosis of GUTB is made on the basis of the histologic pattern or on the detection of *M. tuberculosis* complex by PCR.

However, the biologic activity of tuberculosis can only be assessed by cultivating mycobacteria. In a study of 118 patients suffering mostly from renal GUTB,<sup>18</sup> tissue specimens were minced and dispersed in 0.9% sterile saline and examined by

microscopy, culture, and animal experiment. Mycobacteria were detected in 34 of 118 tissue samples (29%). The renal tissue samples were divided into two groups, one before and one after a 3-month course of antituberculosis treatment. Interestingly, the latter group demonstrated a higher amount of detected mycobacteria (Table 18.1). This finding clearly questions the use of short-term treatment modalities in GUTB. The results also show that direct proof of the presence of mycobacteria makes possible a reliable assessment of the biologic activity of GUTB, which is desirable for treatment planning and therapy control.

### *Treatment*

Medical treatment of GUTB is the treatment of choice. Although different antituberculosis drugs have been introduced, the general therapy regimen for the past 20 years has continued to be a combination of three or four drugs: namely, isoniazid, rifampicin, ethambutol, pyrazinamide, streptomycin, and prothionamide.

The duration of treatment has been reduced in these

**Table 18.1** *Detection of mycobacteria from renal tissue specimens before and after a 3-month course of antituberculosis treatment*

| Antituberculosis treatment | Mycobacteria present | No mycobacteria present |
|----------------------------|----------------------|-------------------------|
| No ( <i>n</i> =26)         | 7 (27%)              | 19 (73%)                |
| Yes ( <i>n</i> =40)        | 14 (35%)             | 26 (65%)                |
| Summary ( <i>n</i> =66)    | 21 (32%)             | 45 (68%)                |

**Table 18.2** *Antituberculosis drug regimens in genitourinary tuberculosis*

| 6-month regimen   | 9-month regimen   |
|---|---|
| 2–3 months daily isoniazid+rifampicin+ethambutol (pyrazinamide) | 2–3 months daily isoniazid+rifampicin 4-ethambutol (pyrazinamide) |
| 3–4 months twice a week isoniazid+rifampicin                    | 6–7 months twice a week isoniazid 4-rifampicin                    |

combination therapies from 2 years down to 9 or only 6 months (Table 18.2). The first step is daily treatment with three or four drugs over 6–12 weeks, followed by a two-drug regimen (mostly isoniazid and rifampicin) twice a week over 3 months or 6 months.

A serious problem at present is resistance to the primary drug in a large number of patients with tuberculosis. In a study from the Russian Research Institute of Phthisiopulmonology,<sup>19</sup> 50 isolates of *M. tuberculosis* obtained from patients referred from various parts of Russia were analyzed by PCR and sequenced to study the mechanism of rifampicin resistance. Drug resistance was detected in 33 patients out of the 50 from whom cultures were isolated. Most of the isolates were resistant to rifampicin (*n*=25), isoniazid (*n*=14), and streptomycin (*n*=7). Multidrug resistance was common. Only 6% of the isolates were resistant to one drug, whereas resistance to two, three, four, and five drugs was seen in 14, 32, 40, and 8%, respectively. Fully susceptible isolates

were derived from only 17 patients. In rifampicin-resistant strains, a number of previously unrecognized genetic alterations (point mutations and deletions) were found in the *rpoB* locus. The *rpoB* locus is responsible for a high level of rifampicin resistance ( $>500 \mu\text{g/ml}$  in egg-based medium).

*Mycobacterium bovis* harbors a primary resistance to pyrazinamide and is found in a high percentage of patients with GUTB. In clinical practice, pyrazinamide should be avoided in those cases not only because of the likelihood of primary resistance but also because of the induction of hyperuricemia, which might be detrimental in patients with GUTB.

Surgery as a treatment option has clearly lost its importance, but it might be indicated in complicated GUTB (obstruction, abscess, etc.) or secondary urinary tract infections such as pyelonephritis or nephrolithiasis.

Surgical interventions are needed only in cases with complications (obstruction, abscess, hypertension). Minimally invasive procedures (laparoscopy, percutaneous nephrostomy, stents) should be used.

### Conclusion



**Figure 18.6** Tuberculous ‘pyonephrosis’ with extensive caseous necrosis and renal parenchymal destruction.

Despite advances in medical treatment, tuberculosis has not lost its importance, especially in Third World countries. This is partly as a result of the high incidence of HIV infections and increasing numbers of patients with AIDS.

Current antituberculosis drugs are well known and have been extensively studied for years. These drugs remain highly effective, but the number of drug-resistant strains is increasing, necessitating close monitoring of the effectiveness of therapy in each and every patient. A 6-month course of antituberculous treatment is a minimum requirement for patients with GUTB and should not be shortened.

## Renal and perirenal abscesses with percutaneous drainage

Renal and perirenal abscesses are collections of purulent material that lie within or near renal parenchyma. In contrast to the gram positive cocci organisms seen prior to the advent of widespread antibiotics, offending organisms are most commonly gram-negative bacteria including *E. coli*, *Proteus mirabilis*, and *Klebsiella*. Diagnosis is made by clinical suspicion and confirmation with CT or ultrasound, which has a diagnostic accuracy greater than 90%.<sup>20-21</sup> Although there is evidence that small renal and perirenal abscesses in stable immunocompetent patients can be controlled with parenteral antibiotic therapy only<sup>21-23</sup>, traditional teaching on abscesses demands adequate drainage of purulent material. In many cases, the effectiveness, rapidness, and ease of percutaneous aspiration and drainage have precluded the need for more invasive and morbid open procedures. There is also the added benefit of immediate abscess cultures, as urine and blood cultures frequently fail to demonstrate the offending organism (33% and <50%, respectively).<sup>24</sup> Additionally percutaneous drainage can improve clinical condition so that a subsequent elective nephrectomy can be performed with fewer complications.<sup>25</sup>

The procedure is performed under intravenous sedation and local anesthetic. Descriptions of technique and types of catheters have slight variations, but generally include percutaneous introduction of a small gauge finder needle under CT or ultrasound guidance. Once the needle confirms localization with aspiration of purulent fluid, a larger catheter via a guide wire or trocar is placed. These catheters may be placed on gravity drainage, suction drainage, or removed (percutaneous aspiration). Double lumen catheters permit infusion of saline or antibiotics, and are less prone to clogging.<sup>26,27</sup> On occasion, placement of a nephrostomy tube may help facilitate drainage of the collecting system if the abscess is associated with infected stone burden and obstruction.

Care should be taken to avoid the pleural cavity during the drainage procedure as complications such as pneumothorax and empyema may necessitate further interventions (chest thoracostomy). To avoid incidental violation of the pleural cavity, introduction of the finder needle should be infracostal to the 12th rib with the needle tip directed cephalad (even if the fluid collections are near the upper pole). It is also important to avoid bowel injury and the peritoneal cavity; therefore access should be medial to the posterior axillary line.

The three most important determinants to the success of percutaneous drainage are size of the abscess; consistency of the fluid; and the presence of loculations. Large abscesses are more likely to need repeat percutaneous drainage procedures and proceed to open surgical intervention. The literature suggests that all renal and perinephric abscesses >5 cm should undergo open surgical drainage.<sup>21,23</sup> However, consideration should be given to initial percutaneous drainage given its high safety profile and low morbidity. Repeat percutaneous drainage is often necessary. Once these options fail, open surgery with placement of large drains or nephrectomy may be merited. Secondly, viscous fluid collections can be difficult to drain when a small diameter catheter is placed via percutaneous approach. The presence of intralesional air heralds a thick collection and is more likely to require an open procedure. Thirdly, loculations and septations in a renal abscess prevent full drainage of purulence and can decrease the success rate from 80% to 45%.<sup>28</sup> Other factors that make percutaneous drainage unsuccessful include fungal infections, the presence of calcifications, infected hematoma, and enteric fistula.

Percutaneous drainage over the past 20 years has changed the treatment paradigm of renal and perirenal abscesses. Overall success rate has been reported to range from 82–97%.<sup>20,21,23</sup> Complication rates have been reported up to 10% and include urosepsis, bleeding, persistent infection, and secondary nephrectomy.<sup>20,27–29</sup> Percutaneous drainage of renal and perirenal abscess, however, remains a safe and effective intervention. We recommend the use of IV antibiotics and percutaneous drainage for lesions <5 cm, and consideration of percutaneous drainage prior to open incision and drainage for lesions greater than 5 cm. Most lesions less than 3 cm will also need percutaneous drainage. Percutaneous drainage of renal and perirenal abscesses also has a role as an adjunct prior to interval nephrectomy (open or laparoscopic).

### **Laparoscopic nephrectomy on infected kidney, xanthogranulomatous pyelonephritis and tuberculosis**

#### *Introduction*

Laparoscopic nephrectomy has been performed for various benign and malignant renal diseases. The advantages of the laparoscopic approach are decreased morbidity and convalescence time. The spectrum of laparoscopic nephrectomy for benign renal conditions includes renovascular diseases, hydronephrosis, reflux nephropathy, renal stones, renal dysplasia, and infectious and inflammatory conditions such as chronic pyelonephritis, xanthogranulomatous pyelonephritis (XGP), and tuberculosis. While the laparoscopic management of nonfunctioning atrophic kidneys and renal atrophy secondary to renovascular hypertension is straightforward, infectious conditions may present significant challenges with respect to increased operative morbidity and detract from the advantage of the laparoscopic approach.<sup>30,31</sup> Based on the collective experience of the study on the laparoscopic Working Group of the German Urological Association, cases with severe perinephric adhesions, such as XGP and tuberculosis proved to be difficult to accomplish via a laparoscopic route unless the surgeon has over 10 years experience in laparoscopic nephrectomy.<sup>31</sup>

#### *Technique*

Laparoscopic nephrectomy was initially described in 1991 by Clayman et al.<sup>32</sup> Commonly, laparoscopic nephrectomy is performed by the transperitoneal approach. This is because the transperitoneal route offers a large working space and well-defined anatomic landmarks. A retroperitoneal access is mostly used for open urological procedures as it is associated with less postoperative morbidity. In laparoscopy, the retroperitoneal approach has had its advocates. Gaur<sup>33</sup> developed a balloon dissection technique of the retroperitoneum. This technique was successfully used for multiple retroperitoneal procedures, including simple nephrectomy, also on infected kidneys.<sup>33–35</sup>

For inflammatory renal conditions, transperitoneal as well as retroperitoneal approaches were performed.

Kim et al<sup>36</sup> reported on laparoscopic nephrectomy in 13 patients with tuberculous nonfunctioning kidney. Nine patients underwent the transperitoneal approach, whereas

Hemal et al<sup>37</sup> treated all their 9 patients with nonfunctioning tuberculous kidney with retroperitoneoscopic nephrectomy, 2 patients requiring conversion to open surgery.

### Results

Literature shows a different outcome of laparoscopic<sup>30,31,34,38,39</sup> Rassweiler et al<sup>31</sup> reported that 90% of laparoscopic nephrectomies were performed from a benign pathologic condition. The conversion rate to open surgery was 10.3%, including 4 cases of tuberculosis and 2 cases of XGP. By contrast, the conversion rate of renal tuberculosis, post-traumatic renal atrophy, infarcted kidney as well as XGP was 89% (Table 18.3).

Another study<sup>31</sup> of 100 cases of laparoscopic nephrectomy, including 42 patients with a variety of inflammatory conditions—e.g. XGP, pyonephrosis and previous surgery—demonstrated that those patients were at a significantly higher risk for complications and conversion to open surgery.

Shekarriz et al<sup>38</sup> reviewed their results of laparoscopic nephrectomy in 12 patients with inflammatory renal conditions (8 chronic inflammation/fibrosis, 3 XGP, 1 tuberculosis). The mean estimated blood loss was  $155 \pm 163$  ml, the mean operative time  $284 \pm 126$  min. In comparison with operative data on noninflammatory renal conditions (9 patients), there was a significant difference of mean blood loss between the inflammatory and the noninflammatory groups ( $p < 0.01$ ). Only in two cases of the inflammatory group was a conversion to open surgery needed.

In XGP as an atypical form of chronic renal infection, open nephrectomy is the treatment of choice. Bercowsky et al<sup>39</sup> compared their experience with laparoscopic nephrectomy (5 cases) for histologically confirmed XGP with the open approach (4 cases). For the laparoscopic group, the average operating time was 360 min, average blood loss was 260 ml, and complications occurred in 60% of patients (1 conversion to open, 1 ileus, 1 pulmonary embolus). In comparison, for the open group the average operating time was 154 min, the average blood loss was 438 ml, and there were no complications.

Laparoscopic nephrectomy for nonfunctioning tuberculous kidneys was relatively contraindicated because of difficulties in dissecting the dense fibrotic adhesions, the high conversion rate, and the risk of spillage of caseous material with subsequent dissemination of the disease. Kim et al<sup>36</sup> reviewed the three center results of efficacy and safety of laparoscopic nephrectomy for renal tuberculosis in 13 patients. Nine patients underwent the transperitoneal approach and four patients the retroperitoneal

**Table 18.3** *Results of laparoscopic nephrectomy on infected kidneys*

| Author                                 | Pathologic condition                                | Laparoscopic              |                      |                              | Open                      |                      |
|--|---|---------------------------|----------------------|------------------------------|---------------------------|----------------------|
|  |   | Mean operating time (min) | Mean blood loss (ml) | Conversion (No. of patients) | Mean operating time (min) | Mean blood loss (ml) |
| Rassweiler et al <sup>31</sup> (n=482) | Mixed, including: • XGP—3 patients • Tuberculosis—5 | 188                       |                      | 46 (7)                       |                           |                      |

| patients                               |              |     |     |   |     |     |
|--|--------------|-----|-----|---|-----|-----|
| Shekarriz et al <sup>38</sup> (n=12)   | Inflammatory | 284 | 155 | 2 |     |     |
| Bercowsky et al <sup>39</sup> *(n=5/4) | XGP          | 360 | 260 | 1 | 154 | 438 |
| Kim et al <sup>36</sup> (n=13)         | Tuberculosis | 268 | 227 | 1 |     |     |
| Hemal et al <sup>37</sup> (n=919)      | Tuberculosis | 103 | 101 | 2 | 92  | 123 |

\*Laparoscopic/open. XGP=Xanthogranulomatous pyelonephritis.

approach. There were no significant intraoperative and postoperative complications. Conversion to open surgery was needed in only 1 patient.

In another study, Hemal et al<sup>37</sup> compared the results of retroperitoneoscopic nephrectomy with open surgery for tuberculous nonfunctioning kidneys. Nine patients underwent retroperitoneoscopic nephrectomy for tuberculous nonfunctioning kidneys and 9 patients underwent open nephrectomy. The two initial cases of retroperitoneoscopic nephrectomy required conversion to open surgery. In retroperitoneoscopic nephrectomy, compared with open surgery, the mean hospital stay was significantly shorter ( $p<0.05$ ) and the patients required significantly less time to return to work (3 v 7 weeks,  $p<0.01$ ).

The treatment of choice for nonfunctioning TB: kidney is transperitoneal laparoscopic nephrectomy. Successful completion of the procedure has exceeded 90%.

In conclusion, laparoscopic nephrectomy for infected nonfunctioning kidney can be challenging. However, as the experience of the surgeon increases, so successful operative outcomes increase.

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## Lower urinary tract infection and prostatitis

Constantine Harris and Michel A Pontari

### Minimally invasive approaches to prostatitis

#### *Introduction*

A number of minimally invasive techniques have been applied toward the treatment of prostatitis. Most of these techniques had their start in the treatment of benign prostatic hyperplasia (BPH) or other voiding disorders and were subsequently applied toward the treatment of prostatitis.

#### *Classification*

Chronic prostatitis is a syndrome characterized by pelvic pain with or without voiding symptoms. The traditional classification of prostatitis included acute prostatitis, chronic bacterial prostatitis, chronic nonbacterial prostatitis and prostatodynia. In 1995 the National Institutes of Health (NIH) developed a new classification scheme for prostatitis.<sup>1</sup> Only 5–10% of all cases of prostatitis are caused by bacteria.<sup>2</sup> In the NIH classification, these are category I, acute bacterial prostatitis, and category II, chronic bacterial prostatitis. The vast majority of men with symptomatic prostatitis fall into category III, or chronic pelvic pain syndrome (CPPS). This condition accounts for up to 2 million outpatient visits per year, up to 8% of visits to urologists and 1% of primary care visits.<sup>3</sup> Category III includes the old classes of chronic nonbacterial prostatitis and prostatodynia. This category can be further divided into IIIA (inflammatory) and IIIB (noninflammatory). Category IV was created to include patients who are asymptomatic but have histologic evidence of prostatitis on biopsy (Table 19.1).

Some of the more common pathogens causing bacterial prostatitis are *Escherichia coli*, *Klebsiella*, *Enterobacter*, *Proteus* and *Pseudomonas*. Patients with category I present with suprapubic discomfort, dysuria, often with voiding difficulty and fever. Treatment includes antibiotics and urinary drainage. Category II or chronic bacterial prostatitis is characterized by relapsing episodes of bacterial cystitis, usually with the same organism seen on urine cultures. These patients are treated with courses of oral antibiotics, and are usually symptom free between episodes. The vast majority of cases will be category III. These patients have pelvic pain, with or without voiding symptoms. The current NIH definition is pelvic pain for at least 3 months' duration. The etiology of this type of prostatitis is unknown, but many causes have been proposed including autoimmune, neurogenic, and infectious.<sup>4–6</sup>

**Table 19.1** *The NIH prostatitis classification system*

|               |  |
|---------------|--|
| Category I    | Acute bacterial prostatitis (acute infection of the prostate)  |
| Category II   | Chronic bacterial prostatitis (recurrent infection of the prostate)  |
| Category III  | Chronic abacterial prostatitis/chronic pelvic pain syndrome (no demonstrable infection)  |
| Category IIIA | Inflammatory (White blood cells in semen/EPS/VBU)  |
| Category IIIB | Noninflammatory (no white blood cells in semen/EPS/VBU)  |
| Category IV   | Asymptomatic, inflammatory prostatitis (no subjective symptoms detected either by prostate biopsy or the presence of white blood cells in EPS during evaluation for other disorders) |

EPS, expressed prostatic secretions; VBU, Reproduced with permission from Textbook of prostatitis, published by Isis Medical Media Ltd.

The evaluation for prostatitis should include a detailed history and physical examination. In patients with category I, urine and blood cultures should be obtained. Those who don't initially respond to antibiotics should have imaging studies to look for a prostatic abscess. In patients with category II, localization cultures should be obtained. The traditional Meares-Stamey 4 glass test—VB1, VB2, EPS (expressed prostatic secretions), VB3—or the simpler Pre and Post Massage Test (PPMT) can be performed<sup>7</sup> (Figure 19.1). In patients with category III, the NIH Chronic Prostatitis Symptom Index is a validated selfadministered index which is useful to measure symptoms<sup>8</sup> (Figure 19.2). The index has three domains: pain, urinary symptoms, and quality of life. Scoring can be used to identify areas to target in the history and clinically to follow patient progress. The use of the 4 glass localization cultures for category III has been called into question by the findings that asymptomatic men have a similar amount and localization of bacteria on this test as do symptomatic men with category III.<sup>9</sup> However, the 2 or 4 glass localization can be useful to rule out category II. A urine cytology should be obtained to rule out bladder cancer/CIS (carcinoma in situ) as a cause of the persistent voiding symptoms and dysuria.<sup>10</sup> Other recommended tests include a urine flow rate and residual urine determination by ultrasound to rule out urinary retention. Optional studies that may be needed in selected patients include semen cultures, urodynamic studies, and computed tomography (CT) or magnetic resonance imaging (MRI) imaging of the pelvis and prostate.<sup>11</sup> The main goal of the evaluation of patients with category III or CPPS is to try to find a treatable cause of the symptoms. Unfortunately, in the vast majority of men, no such cause will be identified and treatment is therefore empiric and directed at symptom relief instead of cure of the underlying problem.

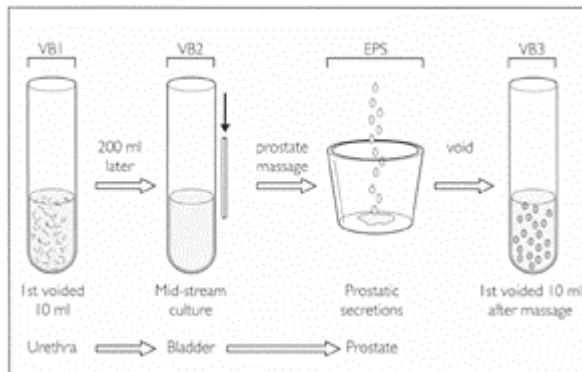
Antibiotics are the mainstay of treatment for category I and II prostatitis. They are also frequently used for category III. One course of antibiotics for 4 weeks is recommended for these patients. If the patient responds to the initial course, then therapy can be continued for an additional 2–4 weeks.<sup>12</sup> The fluoroquinolones are the antibiotics of choice. What is not recommended are multiple repeated courses of antibiotics after the initial treatment, in the absence of positive cultures. Alpha-blockers are frequently useful

for chronic prostatitis.<sup>13</sup> Anti-inflammatory medications round out the most frequently used therapies.<sup>14</sup> There are many other oral therapies which can be useful. In patients with the predominant symptom of pain, oral analgesics such as tricyclic antidepressant medications and antiepileptics such as gabapentin can be tried. Finasteride has been reported to have some success in CPPS.<sup>15</sup> Anticholinergics and even synthetic heparinoids such as pentosan polysulfate can be used in patients with voiding symptoms.<sup>16</sup> The treatments used for CPPS are very similar to those used for interstitial cystitis.<sup>17</sup> Pelvic floor physical therapy is also a good option in these patients.<sup>18</sup> A key point to remember prior to initiating minimally invasive treatments is that given that almost all treatment of CPPS is empiric, it is important to exhaust all possible noninvasive treatments prior to any invasive treatment. Also, one must remember that CPPS likely represents an end symptom complex that probably has multiple etiologies, not all of which are caused by the prostate.

### Minimally invasive treatments

#### *Microwave hyperthermia and thermotherapy*

Heat therapy using microwaves has been applied to the prostate for the treatment of BPH since 1985.<sup>19</sup> Early treatments were termed hyperthermia and referred to heating



**Figure 19.1** Meares—Stamey 4-glass test of localization cultures of the lower urinary tract in the male. The first voided 10 ml of urine is collected, sent for culture, and denoted VB1. In a separate culture container, the next 200 ml is collected, submitted for culture, and denoted VB2. The patient then undergoes prostatic massage, where

the expressed prostatic secretions (EPS) are cultured. Then the patient voids, the specimen is submitted for culture, and denoted VB3. For diagnosis of category 2 (chronic bacterial prostatitis), the bacteria counts in the EPS specimens must exceed by greater than equal to tenfold the combined counts of VB1 and VB2. (Reproduced with permission from the Textbook of prostatitis, published by Isis Medical Media Ltd.)

| Pain or Discomfort  |           | Yes                      |                          | No                       |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
|---|-----------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|---|--------------------------|---|--------------------------|--------------------------------|--------------------------|---|--------------------------|---|--------------------------|---|--------------------------|---|--------------------------|----|
| 1. In the last week, have you experienced any pain or discomfort in the following areas?  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| a. Area between rectum and testicles (perineum)   |           | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| b. Testicles  |           | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| c. Tip of the penis (not related to urination)  |           | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| d. Below your waist, in your pubic or bladder area  |           | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| 2. In the last week, have you experienced:  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| a. Pain or burning during urination?  |           | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| b. Pain or discomfort during or after sexual climax (ejaculation)?  |           | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| 3. How often have you had pain or discomfort in any of these areas over the last week?  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/>  | Never     |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/>  | Rarely    |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/>  | Sometimes |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/>  | Often     |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/>  | Usually   |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/>  | Always    |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| 4. Which number best describes your AVERAGE pain or discomfort on the days that you had it, over the last week?                                   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/>  | 0         | <input type="checkbox"/> | 1                        | <input type="checkbox"/> | 2                        | <input type="checkbox"/> | 3 | <input type="checkbox"/> | 4 | <input type="checkbox"/> | 5                              | <input type="checkbox"/> | 6 | <input type="checkbox"/> | 7 | <input type="checkbox"/> | 8 | <input type="checkbox"/> | 9 | <input type="checkbox"/> | 10 |
| NO PAIN   |           |                          |                          |                          |                          |                          |   |                          |   |                          | PAIN AS BAD AS YOU CAN IMAGINE |                          |   |                          |   |                          |   |                          |   |                          |    |
| Urination   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| 5. How often have you had a sensation of not emptying your bladder completely after you finished urinating, over the last week?                   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Not at all   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Less than 1 time in 5  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Less than half the time  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> About half the time  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> More than half the time  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Almost always  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| 6. How often have you had to urinate again less than two hours after you finished urinating, over the last week?                                  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Not at all   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Less than 1 time in 5  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Less than half the time  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> About half the time  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> More than half the time  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Almost always  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| Impact of Symptoms  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| 7. How much have your symptoms kept you from doing the kinds of things you would usually do, over the last week?                                  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> None   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Only a little  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Some   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> A lot  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| 8. How much did you think about your symptoms, over the last week?  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> None   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Only a little  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Some   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> A lot  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| Quality of Life   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| 9. If you were to spend the rest of your life with your symptoms just the way they have been during the last week, how would you feel about that? |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Delighted  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Pleased  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Mostly satisfied   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Mixed (about equally satisfied and dissatisfied)   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Mostly dissatisfied  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Unhappy  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| <input type="checkbox"/> Terrible   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| Scoring the NIH-Chronic Prostatitis Symptom Index Domains   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| Pain: Total of items 1a, 1b, 1c, 1d, 2a, 2b, 3, and 4 = _____   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| Urinary Symptoms: Total of items 5 and 6 = _____  |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |
| Quality of Life Impact: Total of items 7, 8 and 9 = _____   |           |                          |                          |                          |                          |                          |   |                          |   |                          |                                |                          |   |                          |   |                          |   |                          |   |                          |    |

**Figure 19.2** The NIH Chronic Prostatitis Symptom Index (NIH-CPSI) is utilized to measure

symptoms. This index is a 9 question test broken down into three domains: (1) pain; (2) urinary symptoms; and (3) quality of life. (Reproduced with permission from the Textbook of Prostatitis, published by Isis Medical Media Ltd.)

the prostate to 42–44°C. Thermotherapy refers to heating to temperatures higher than 45°C. Microwaves comprise the 300–3000 MHz range of the electromagnetic spectrum. BPH tissue requires heating to greater than 44°C for at least 30 min to cause coagulation necrosis. Microwave energy has been shown to have a bactericidal effect in vitro on two bacteria known to cause prostatitis, *E. coli* and *Enterobacter cloacae*.<sup>20</sup> The bactericidal effects of microwaves, delivered by a Prostatron 2.0 were independent of heat production. These authors suggest that there may be a role for transurethral microwave thermotherapy (TUMT) in the treatment of chronic bacterial prostatitis. A similar study showed that microwave energy delivered with a Prostatron device is more efficient at killing cultured *E. coli* than heat alone.<sup>21</sup> Therefore, there may be a role for thermotherapy in patients with documented bacterial prostatitis, who experience multiple symptomatic recurrences despite antibiotic therapy including a course of prophylaxis for 3–6 months. This may also be useful in the patient with bacterial prostatitis who has extensive allergies to antibiotics.

The therapeutic mechanism of thermotherapy for CPPS is not completely understood. Perachino and coworkers demonstrated the effects of transurethral microwaves on prostate tissue by performing open prostatectomy after TUMT and evaluating the specimens using histologic and immunohistochemical stains.<sup>22</sup> They found marked damage and disappearance of nervous fibers. Based on these findings, they propose that TUMT may induce a long-term alpha-blockade. This is consistent with the effects seen by alpha-blockers on this condition.<sup>13</sup>

### **Transrectal thermotherapy**

Microwave hyperthermia of the prostate for the treatment of prostatitis was first applied transrectally. Microwave hyperthermia produces intraprostatic temperatures less than 45°C. Servadio et al described the use of transrectal microwave hyperthermia in 21 patients that had chronic abacterial prostatitis. They demonstrated significant improvements in symptoms at up to 24 months followup.<sup>23</sup> Servadio and Leib subsequently reported similar encouraging results in 45 patients;<sup>24</sup> three-quarters of patients reported either complete loss of symptoms or partial response. Montorsi and coworkers administered transrectal microwave hyperthermia in 54 patients who had failed conventional therapies. They found that 50% of patients reported improvement in quality of life after a mean of 26 months follow-up.<sup>25</sup> Similar improvements were reported in other trials.<sup>26–28</sup> Shah and coworkers reported on a double-blind placebo-controlled trial of transrectal microwave hyperthermia.<sup>29</sup> Fifteen patients were in the

treatment group and 55% showed improvement after 3 months compared to only 10% of the placebo group.

### **Transurethral microwave thermotherapy**

TUMT was first introduced by Devonec et al as a treatment for BPH.<sup>30</sup> It has since been shown to be a safe and effective treatment for BPH.<sup>31,32</sup> An early trial applied TUMT to 19 patients with nonbacterial prostatitis (leukocytosis in EPS) and 5 patients with prostatodynia (no leukocytosis in EPS).<sup>33</sup> They found a favorable response rate (50%) among nonbacterial prostatitis patients but little benefit in the prostatodynia group. Patients were treated with a single 1-hour session and evaluated after 3 months. Choi and coworkers also describe the use of TUMT in patients with chronic nonbacterial prostatitis and prostatodynia.<sup>34</sup> They also applied a single 1-hour session of TUMT. At 1-year follow-up in prostatodynia patients, they found a 35% complete response rate, and a 41% partial response rate. Among nonbacterial prostatitis patients, there was a 23% complete and 43% partial response rate.

A randomized trial of TUMT versus sham therapy with a small number of patients reported significant improvement of symptoms in the treated patients.<sup>35</sup> While 70% of the treatment group showed significant improvement, only 10% of the same surgery group showed significant improvement. Several other nonrandomized studies have also reported favorable results with TUMT for nonbacterial prostatitis.<sup>36,37</sup>

Several microwave devices are available, including the Prostatron (2.0 and 2.5), ProstaLund™, and Prostatecare. The most commonly used device in clinical trials has been the Prostatron 2.0. Temperature monitoring of the urethra, prostate, and rectum are performed during TUMT. The temperature limit for the urethra should be 45°C to minimize the incidence of urethral injury. Urethral cooling is accomplished with the urethral cooling catheter. High-energy and low-energy TUMT are available. Low-energy protocols heat the prostate up to 50°C whereas high-energy protocols heat it up to 75°C. Use of high-energy TUMT has not been described in the treatment of prostatitis. Thermotherapy treatments consist of a single 1-hour treatment. Complication rates for TUMT when used for treatment of BPH include 3% acute incontinence, 13% infection, and 11% urinary retention of a mean duration of 17.5 days.<sup>38</sup> Higher-energy TUMT protocols (Prostatron 2.5) have been associated with a higher incidence of urinary retention. To minimize this problem, a Foley catheter can be left in temporarily. One group has described the use of a temporary biodegradable urethral stent in the treatment of BPH patients.<sup>39</sup>

### *Transurethral needle ablation*

Transurethral needle ablation (TUNA) is a minimally invasive technique developed for the treatment of BPH. It delivers low-level radiofrequency (RF) energy at 490 kHz to heat tissue and selectively ablate prostatic tissue. Tissue is heated to 100°C, while maintaining urethral temperatures below 42°C. It has been demonstrated that RF energy results in severe thermal damage to intraprostatic nerve fibers.<sup>40</sup> The suggested therapeutic mechanism of action may be a long-term denervation of alpha-receptors and/or sensory nerves. RF ablation of the prostate is performed on an outpatient basis

under local anesthesia. Risks of the procedure include urinary retention and irritative voiding symptoms.

While TUNA has been shown to be effective in the treatment of BPH, reports on its use for treatment of chronic prostatitis and CPPS have been mixed. A pilot study performed on 7 patients reported complete resolution of symptoms in 4 patients and partial resolution in 3 patients.<sup>41</sup> All patients had a decrease in the leukocyte count in EPS after 1 month. A prospective nonrandomized trial reported excellent results in terms of improved symptom score and decreased leukocyte count in expressed prostatic secretions.<sup>42</sup> This study included 42 patients and followed them for 3 months after TUNA. Leskinen and coworkers investigated the effectiveness of TUNA versus sham treatment in patients with CPPS.<sup>43</sup> This was a randomized trial with 25 patients in the treatment arm and 8 patients in the sham group. Follow-up was at 3, 6, and 12 months after treatment. In this study, TUNA and sham treatment both significantly reduced prostatitis and urinary symptoms and no statistical differences were found between the two groups.

### *Laser therapy*

Interstitial laser therapy involves application of laser energy directly into the target tissues, which results in coagulation necrosis of prostate tissue. It has been studied more extensively for the treatment of BPH but has also been applied for the treatment of prostatitis. The Nd:YAG laser has a wavelength of 1064 nm and is delivered through small semiflexible fibers. Suzuki et al reported results using the PROSTALASE™ Nd:YAG laser device. Balloon laser hyperthermia with a target temperature of 43°C was performed in a small number of patients (5) with chronic nonbacterial prostatitis. They reported symptomatic improvement as well as decreased leukocyte count in expressed prostatic secretions in 4 out of 5 patients.<sup>44</sup> Serel and coworkers, reporting the results of Nd:YAG laser therapy on a group of 30 patients with chronic abacterial prostatitis or prostatodynia,<sup>45</sup> found statistically significant improvements in objective measures such as IPSS (International Prostate Symptom Score), quality of life index, and EPS leukocyte count.

### **Balloon dilatation**

Transurethral balloon dilatation for the treatment of abacterial chronic prostatitis and prostatodynia was employed by Lopatin et al.<sup>46</sup> They treated 7 patients diagnosed with functional urinary outlet obstruction as well as chronic prostatitis or prostatodynia and showed an improvement in voiding symptoms. Dilatation was performed with a 25 mm urethroplasty balloon catheter inflated to 3.5 atm pressure for 20 min. All patients reported improvement in voiding symptoms with follow-up of 1–5 months. Pain was not assessed in this study. Transurethral RE hot balloon thermal therapy combines the techniques of balloon dilatation with RE heating of the prostate.<sup>47</sup> They found a high complication rate and no patient reported improvement at 9 months follow-up.



*Sacral nerve stimulation*

One of the most promising new techniques is transforaminal sacral nerve stimulation. This has been shown to benefit patients with chronic voiding dysfunction including urge incontinence and urgency-frequency syndrome.<sup>48</sup> This technique has recently been applied toward the treatment of patients with chronic intractable pelvic pain. The use of sacral nerve stimulation is based on the hypothesis that the pain is neural in origin. Among the data to support a neurologic hypothesis are that given by Zermann et al.<sup>5</sup> They found significant abnormalities in the coordination of voiding and the activity in the pelvic floor/external urethral sphincter in over 80% of men with symptoms of pelvic pain. This kind of dysfunction is classically found in patients with suprasacral spinal cord lesions, such as patients with a complete spinal cord injury or men with spinal cord plaques from MS (multiple sclerosis). Whether these men have a subclinical neural injury in the spinal cord that would contribute to such dyssynergy, and thus pelvic pain, is as yet unanswered. The technique is a two-step process that involves a prosthetic neurostimulator and the leads that go into the sacral foramina. Initially, a test lead was used, but more recently the permanent leads are placed and attached to a temporary device during the first stage.<sup>49</sup> If the patient responds, the permanent stimulator is then implanted subcutaneously at a second procedure. Early results with implantable sacral nerve stimulators in patients with chronic pelvic pain have been promising.<sup>50</sup> Of the 10 patients in the study by Siegel et al, 6 patients reported significant improvement in pelvic pain symptoms at 19 months follow-up.<sup>51</sup>

*Transurethral resection of the prostate*

Transurethral resection of the prostate (TURP) has been advocated for treatment of chronic bacterial prostatitis in carefully selected patients.<sup>52,53</sup> Surgery is performed with the intent of removal of the gland down to the true capsule. In the larger of the two studies (49 patients), twothirds of patients had resolution of symptoms or infections after 1 year.<sup>52</sup> This may be indicated in patients with residual foci of bacterial prostatitis in whom this may be causing either significant recurrent infections or in whom being clear of infection is necessary. Examples include patients who are immunosuppressed, those having recurrent febrile urinary tract infections/acute prostatitis, and in patients with chronic bacterial infection who are otherwise candidates for implantation of an artificial urinary sphincter.

*Transurethral incision of bladder neck*

There is a very small but identifiable subset of patients with CPPS in whom a transurethral incision of the bladder neck (TUIBN) is indicated. These are patients with dyssynergy of the smooth sphincter, or bladder neck. It is important to identify this subset of patients, because, in this group, TUIBN is very successful and can make a marked difference in their symptoms. These patients have evidence of bladder outlet obstruction on videourodynamic studies, with high voiding pressure and low flow. On fluoroscopy, there is a loss of the usual funneled appearance to the bladder neck during voiding.

Instead, there is a very sharp cutoff with a near 90° angle between the bladder neck and the urethra. Clinically, these patients complain of a weak urinary stream, often of long-standing duration. They will sometimes report difficulty urinating in public places, sometimes called 'shy bladder.' Stress can release catecholamines that can act through the abundant alphas receptors in the bladder neck to cause contraction of the muscle. Kaplan and coworkers reported on a series of TUIBN performed: of 31 patients, 30 had marked subjective improvement in symptoms with an increase in maximal urine flow.<sup>54</sup> The technique involves making an incision from just distal to each ureteral orifice, down through the bladder neck to just proximal to the verumontanum. One significant side-effect of this procedure is retrograde ejaculation. This must be thoroughly discussed with males who are still interested in possibly fathering children.

### *Conclusion*

There are multiple options for minimally invasive therapy in the treatment of patients with chronic prostatitis and CPPS. Some such as TUIBN and TURP will have an ongoing role with fairly specific indications in a small subset of patients. Others such as balloon dilation and laser therapy do not appear to be useful enough to warrant continued use. Sacral nerve stimulation is fast becoming an important mode of therapy and has proved to be effective, often in patients who have not responded to many other therapies. More uncertain is the use of 'prostate'-specific therapies such as TUMT and TUNA. Part of the problem is the unclear etiology of the syndrome. Although this symptom complex of pelvic pain and voiding symptoms is called prostatitis, it is not clear that in all patients it has anything to do with the prostate. As our understanding of the pathophysiology of this condition improves, so will our ability to choose appropriate therapy and use the minimally invasive therapies already available to us more wisely.

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## Voiding/neurogenic bladder evaluation and minimally invasive treatment options

Michael Gross and Timothy B Boone

### Introduction

The term neurogenic bladder (NGB) is a misnomer as it encompasses voiding dysfunction caused by the bladder, urethra, or both. The term NGB is applied when there is a known neurologic lesion that manifests itself in the voiding dysfunction and sometimes when there is no other obvious pathologic finding. Accurate diagnosis of the underlying pathology causing the NGB is of paramount importance, as is investigation of comorbidities associated with the voiding dysfunction. Because voiding dysfunction may affect the entire urinary system, a thorough evaluation of the upper and lower urinary tract is required in order to choose the best intervention for a given patient.

After a proper neurologic evaluation is completed, most patients need to undergo urodynamic evaluation. Urodynamic testing will vary, depending on the etiology of the voiding dysfunction. In general, patients with intact sensation and no overt neurologic disease will require fewer channels of recording and may not need simultaneous fluoroscopic imaging during the test. Accurate urodynamic testing requires verbal interaction with the patient during the study and the skill of the technician to continuously monitor the quality of the recording session. Since many neurologically impaired patients are unable to control micturition or are devoid of sensations arising from the lower urinary tract, the urodynamic testing results will provide the guide for effective bladder management. Detrusor compliance during filling and storage is of paramount importance to protect renal function. Only cystometric testing will provide you with a compliance measurement to accurately assess the safety of bladder storage in neurogenic conditions.

Voiding dysfunction can be secondary to failure to store urine or failure to empty the bladder, and either of these problems can result from bladder or urethral dysfunction. Often, failure of the bladder and failure of the urethra coexist and lead to incontinence. The urodynamic study should be focused on the patient's symptoms and should reproduce the symptoms that affect the patient while pinpointing the mechanism that leads to these symptoms.

Treatment of a patient with NGB should take into consideration the natural history of the underlying pathology (e.g. a patient who has progressive motor function deterioration may not benefit from an artificial urinary sphincter that he will be unable to manipulate later on). All attempts should be made to resolve the voiding dysfunction conservatively. However, conservative treatment is often not available or effective. Surgical intervention, when required, should offer lasting management with minimal morbidity. During the last two decades there has been a trend to substitute lessinvasive methods for open procedures

in order to facilitate the patient's rehabilitation. Minimally invasive procedures for NGB can be categorized by the type of bladder or urethral dysfunction that needs to be corrected.

### **Failure to store: bladder**

Urinary incontinence may result from the bladder's inability to store urine. A normal bladder should accommodate a reasonable volume comfortably and maintain low pressure regardless of the increase in volume. Bladder compliance (volume/pressure) is the most important factor in urine storage. The detrusor contracts only when there is a volitional desire to void. Neural imbalance between excitatory and inhibitory pathways may affect the bladder by reducing its compliance, by involuntary detrusor contractions, or by reducing bladder capacity. When the pressure in the bladder overcomes the closure pressure of the sphincteric mechanism, urinary incontinence ensues. The surgical approach to resolve storage failure is directed at attenuating the magnitude of the detrusor contraction, increasing bladder capacity, and improving bladder compliance.

### *Hydrodistention*

Hydrodistention for irritative bladder symptoms was introduced in 1930 and was shown to reduce pain, urgency, and frequency and to increase bladder capacity.<sup>1,2</sup> The mechanism of action is unclear. It has been suggested that hydrodistention leads to ischemic or mechanical damage to submucosal nerve plexuses and stretch receptors, thus leading to attenuation of pain and frequency and to an increase in bladder volume.<sup>3</sup> This theory has been supported by axonal degeneration seen in animal bladders after hydrodistention. Other suggested explanations are reduced proliferation rate of urothelial cells, reduced epidermal growth factors, and increased urinary antiproliferative growth factor.<sup>4-7</sup> A defect in bladder surface mucin was evident in patients with interstitial cystitis that was not apparent in controls.<sup>8</sup> In-vitro and in-vivo studies have demonstrated that hydrodistention leads to increased urothelial excretion of substances such as heparin-binding epidermal growth factor and glycoprotein 51 component of bladder surface mucin and to decreased excretion of antiproliferative growth factors.<sup>9</sup>

Although hydrodistention is a procedure commonly used for treating pain and irritative symptoms, the best regimen and the optimal frequency of treatments are still unknown.<sup>10</sup> In most cases hydrodistention is performed under regional or general anesthesia. In the procedure, the bladder is filled with either sterile water or saline at 80 cmH<sub>2</sub>O pressure until filling stops or until there is leakage around the cystoscope. The bladder is drained after a few minutes. Some urologists drain the bladder and refill it two or three times. Because the method of treatment and the definitions of response are not standardized, the therapeutic efficacy of hydrodistention is difficult to evaluate, with reported success rates ranging from 18% to 77%. Complication rates range from 5 to 10%, with hematuria, dysuria, urinary retention, and bladder perforation being the most common.<sup>9,11-13</sup> The degree and duration of relief obtained in a given patient are unpredictable, but in most cases the procedure offers only temporary relief for a small group of patients.

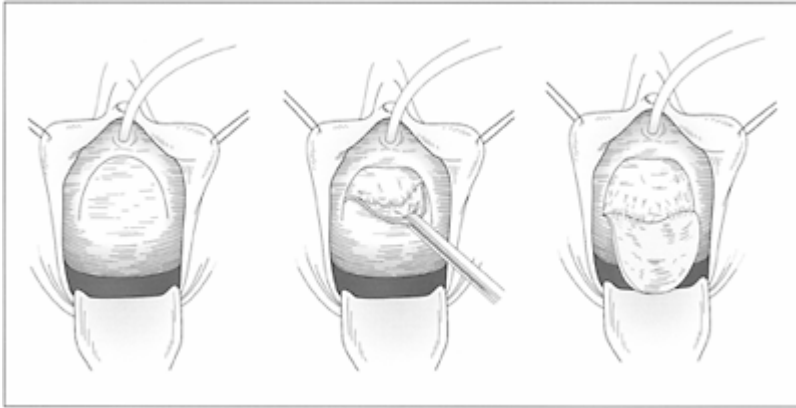
*Ingelman-Sundberg bladder denervation technique*

Ingelman-Sundberg reported his experience with transvaginal peripheral bladder denervation in 1959.<sup>14</sup> In his preliminary series he studied 32 women with detrusor instability, and reported an 88% success rate and a 70% cure rate. The procedure is considered to be most efficacious for patients with symptoms of an overactive bladder. Patients with neurogenic bladders, poor compliance, and interstitial cystitis gain less from the procedure. The assumption is that the procedure causes partial sensory denervation of the trigone. As originally performed, the procedure required extensive dissection of the cervix and the bladder vasculature bilaterally and dissection of terminal pelvic nerve branches. However, the procedure has been modified, with dissection limited to the bladder neck and the subtrigonal area. Use of transvaginal local anesthesia in order to predict therapeutic outcome has achieved favorable results.<sup>15</sup> Transvaginal local anesthesia may be achieved with 5–15 ml of 0.25% bupivacaine injected in the undersurface of the trigone. Resolution of symptoms for several hours indicates that the patient may benefit from the procedure. The procedure is performed under local or regional anesthesia. The vaginal mucosa and the pubocervical fascia are transected off the underlying surface of the bladder (Figure 20.1). The transection at this level causes partial denervation of the bladder. The operation can be performed in approximately 15–30 min and may be done in an outpatient setting. Other studies that employed the Ingelman-Sundberg technique showed longterm success rates of 50–72%.<sup>16,17</sup> Cespedes et al, selecting patients according to their response to transvaginal local anesthesia, demonstrated a cure rate of 64%.<sup>15</sup> Cure was regarded as complete resolution of urge incontinence (UI). About 70% of these women still required some anticholinergic medication after the procedure; in 34% there was only temporary or no response. Recent reports by the same group demonstrated essentially the same results with a longer follow-up.<sup>18</sup> The most frequent complication after the procedure was temporary urinary retention.

*Transvesical injections***Phenol**

Subtrigonal injections of 6% phenol for the treatment of bladder instability were reported in 1969.<sup>19</sup> Injection of this chemical causes neurolysis of terminal pelvic nerve branches as they enter the trigone. Approximately 10–20 ml of phenol is injected through a cystoscope in the submucosal level, bilaterally half way between the bladder neck and each ureteral orifice. The procedure requires either general or regional anesthesia. This treatment modality has yielded mixed results, with some investigators reporting success rates as high as 82–90%.<sup>20,21</sup> Others report poor success rates of 14–19%.<sup>22–24</sup> Some studies attempted to identify subcategories of patients who were most likely to benefit from this procedure. Blackford et al reported a success rate of 82% in women over the age of 55 years and less than 14% in younger women.<sup>20</sup> In other studies patients with multiple sclerosis appeared to benefit most from this procedure.<sup>20,25</sup> In order to improve patient selection, Madjar et al<sup>25</sup> used a transvaginal bupivacaine injection (0.25%) on





**Figure 20.1** Ingelman-Sundberg procedure. (Reproduced with permission from Cespedes et al<sup>15</sup>.)

the assumption that patients who respond to the local anesthetic will later respond to the sub trigonal phenol injection. In their study, 23 of 42 patients (54.7%) responded to the bupivacaine injection. Of all the patients who responded to the phenol injections, 26% had symptomatic relief that lasted more than 3 months. In most cases, relief of symptoms is temporary and lasts from a few weeks to several months. Severe complications, such as vesicovaginal fistula, excoriation of the vaginal wall, and even the need for urinary diversion, were reported in 25–40% in two series.<sup>21,26</sup> However, in these patients, the phenol was mixed in a nonaqueous, glycerol solution that retained the phenol in the perivesical fat for a longer period of time. Because of the high complication rate, many physicians consider previous pelvic surgery or pelvic irradiation to be contraindications for this treatment. The high risk for impotence in males is also a relative contraindication for injection. Very few clinicians use phenol any longer because of the significant risk of tissue damage and complications.

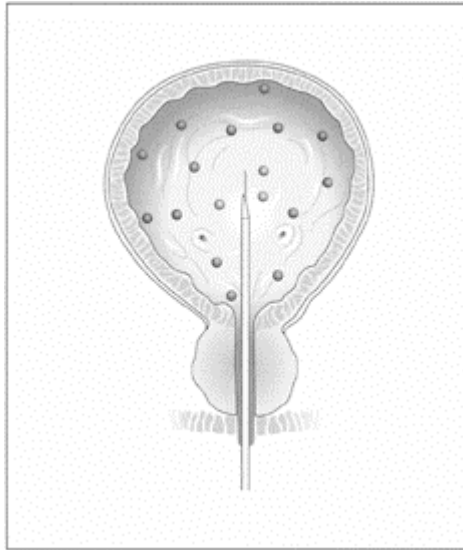
### Botulinum A toxin

Botulinum A toxin (BTX) selectively blocks release of acetylcholine from nerve endings and blocks neural transmission. When injected directly into the muscle, BTX binds to nerve terminals and has a sustained effect.<sup>27</sup> The clinical use of BTX to correct strabismus was pioneered by Scott in 1981.<sup>28</sup> The US Food and Drug Administration (FDA) authorized its use for strabismus, dystonia, and later on for other pathologies such as torticollis and spasticity.<sup>29–31</sup> Schurch et al evaluated the efficacy of injecting BTX directly into the detrusor muscle of spinal cord patients with detrusor hyperreflexia (Figure 20.2).<sup>32</sup> A group of 31 patients with detrusor hyperreflexia and incontinence, despite high doses of anticholinergic medications, were injected with 200–300 units of BTX. Urodynamic study demonstrated an increase in the maximal cystometric capacity and an increase in the volume before incontinence ensued. The patients were able to stop

or decrease the usage of anticholinergics, and stopped experiencing episodes of autonomic dysreflexia. No side-effects were observed. The procedure is performed with the patient under light anesthesia in an outpatient setting. Chancellor et al reported their preliminary data in a group of 50 patients with voiding dysfunction. In this group, 15 were attributed to detrusor hyperreflexia. These patients were injected with 200–300 units of BTX with an overall improvement in more than 80% of the patients and with no adverse effects.<sup>33</sup>

### *Percutaneous neuromodulation*

Electrical stimulation (ES) for the treatment of urinary incontinence has evolved over the last 40 years. In 1963 Caldwell experimented with implantation of an electrode in the periurethral area, with the result that 50% of patients improved or were cured of their incontinence.<sup>34,35</sup> Since



**Figure 20.2** Endoscopic injection of botulinum toxin for detrusor hyperreflexia.

then various techniques have emerged but the response rate has not changed significantly. Although the mechanism of action of ES has been investigated in animal models, the mechanism of action remains unclear in humans.

Several theories have been proposed to explain the effect of ES:

1. Relaxation of detrusor muscle in response to activation of the pudendal nerve.<sup>36</sup> In humans it was shown that sensory input through the pudendal nerve inhibits detrusor

activity.<sup>37</sup> Thus, pudendal nerve stimulation and enhancement of external sphincter tone may serve to control bladder overactivity and facilitate urine storage.

2. Stimulation of afferent sacral nerves in either the pelvis or lower extremities increases the inhibitory stimuli to the efferent pelvic nerve and reduces detrusor contractility.<sup>38</sup> The assumption is that at low bladder volumes there is stimulation of the hypogastric nerve through activation of sympathetic fibers, and at maximal bladder volume direct stimulation of the pudendal nerve nuclei in the spinal cord. Another theory is that there is supraspinal inhibition of the detrusor.<sup>39-41</sup>
3. The bladder responds to neural stimulation initially with rapid contraction followed by slow, longerlasting relaxation. With recurrent, repetitive stimuli there is a decay, and down-regulation of the bladder's response, thus reducing the detrusor's overactivity.

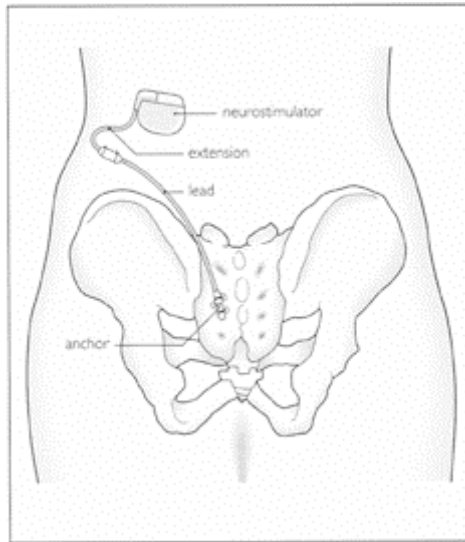
### *Sacral stimulation*

Use of sacral nerve stimulation stemmed from research focusing on the effect of stimulation on the voiding reflex, the influence of sacral nerves on the voiding pattern, and control by the central inhibitory system on micturition.<sup>42,43</sup> It was thought that sacral nerve stimulation induced a reflex inhibitory effect on the detrusor through afferent and efferent fibers in the sacral nerves.<sup>44</sup> As previously stated, the first attempt at neuromodulation through ES was carried out in the 1960s by Caldwell. About three decades later the technique had gained popularity for various lower urinary tract dysfunctions, especially symptoms from uninhibited bladder contractions.<sup>45-49</sup> All candidates are evaluated for a good response to sacral nerve stimulation. The goal of the first stage is to identify the percutaneous location of the sacral nerve that provides the best neuroanatomical response, usually S3. The S3 foramen can be found one finger-breath off the midline at the level of the sciatic notch. Local anesthetic is injected into the skin and the subcutaneous fat with a 2-inch 22gauge needle all the way down to the sacrum. Probing the relevant area with a 21-gauge needle identifies the foramen. Once the foramen is identified, the margins of the opening need to be outlined. The nerve passes at the superior medial aspect of the foramen.<sup>44</sup> Response is evidenced by flexion of the great toe and contraction of the levator ani muscles. In order to facilitate the recognition of the stimulatory effect, two electrodes can be positioned in the urethra and the anal canal. These electrodes record excitation of the external urethral sphincter and the pelvic floor, respectively. The temporary electrode near the sacral nerve is firmly secured and a trial of continuous stimulation is undertaken for a period of 3-7 days. During this time the stimuli are 210 ms, frequency 10 Hz, and amplitude ranging from 0.5 to 10 V is self-managed and adjusted by the patient. Patients who respond favorably and demonstrate a 50% reduction in their episodes of urge incontinence are candidates for surgical implantation of the stimulator (Figure 20.3).

A prospective, multicentered randomized study was carried out from December 1993 to September 1999 utilizing the InterStim System (Medtronic Inc., Minneapolis, Minnesota).<sup>50</sup> A group of 96 patients (85 females, 11 males) were evaluated with an average follow-up time of 30.8 months. Baseline assessment included:

- medical and urological history
- urodynamic testing
- a 3-day voiding diary.

Patients' voiding diaries served as the primary outcome measure. Seventeen of the 96 patients did not benefit from the device, and in 11 of them the device was explanted. Twenty-six patients were defined as cured and had no episodes of UI. Thirty-six had a significant improvement.



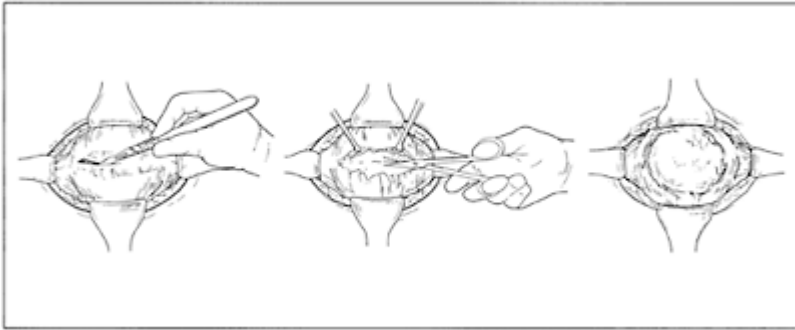
**Figure 20.3** Neurostimulator implant.  
(Courtesy of Medtronic, Inc.,  
Minneapolis, Minnesota.)

With an average follow-up of 30.8 months there was a statistically significant reduction in incontinent episodes, a decrease in the severity of leaking episodes, and a decrease in use of diapers or other absorbent pads ( $p < 0.0001$ ). Statistically significant effects were apparent with an increase in average volume voided per void, increase in maximal voided volume, improved urine stream, improved sensation of 'emptying' post void, decreased number of voids per day, and reduced pelvic discomfort. The majority of patients who had a successful clinical outcome at 6 months demonstrated a sustained beneficial effect later on. Adverse effects were pain at the pulse generator site, which in most cases was caused by interference with a bony structure or belt line, infection, pain at the lead site, and lead migration. Baseline demographic parameters, including age and gender, were not predictive of clinical outcome. While these results are encouraging, it should be emphasized that about 50% of patients do not respond to the test stimulation. Seventeen to twenty percent of those who initially have a favorable response will proceed with implantation later, but will not benefit from the device, and some of them will require an additional procedure to remove the stimulator. In all, about one-third of all patients will have a long-term response to the treatment.

*Detrusor myectomy*

Spontaneously formed bladder diverticuli are seen frequently in patients with neurogenic bladders and in patients with long-standing bladder outlet obstruction. The observation of this phenomenon led Cartwright and Snow in 1989 to suggest deliberate removal of the detrusor muscle in order to create a wide-mouthed iatrogenic diverticulum.<sup>51-52</sup> The goal of the procedure was to increase bladder capacity, to reduce bladder storage pressure, and to attenuate the amplitude of the uninhibited bladder contractions and thus reduce episodes of urinary urgency, urge incontinence, and frequency. The procedure was termed 'autoaugmentation' in contrast with 'augmentation,' which is the term applied to the use of gastrointestinal tissue to augment the bladder. Autoaugmentation was designed to avoid the problems inherent in applying small or large bowel to the genitourinary tract. The procedure is performed with the patient under general or regional anesthesia, and the bladder is exposed extraperitoneally after filling by gravity via a transurethral catheter. Indigo carmine or methylene blue mixed with saline may improve the view and aid in defining the dissection level. The peritoneum is displaced cephalad, and about 25% of the detrusor muscle at the bladder's dome is removed by blunt and sharp dissection, exposing the underlying bulging urothelium (Figure 20.4). The raised detrusor flaps may be anchored to the psoas muscle, although more often than not they are resected.<sup>50-56</sup> Swami et al recommended making a small peritoneal incision in order that the greater omentum may be pulled over and attached to the bladder's anterior wall to prevent inflammatory reaction and fibrosis of the mucosa.<sup>55</sup> In their experience, patients who had an omental flap had less perivesical fibrosis if another intervention was required, whereas patients who had no omental flap were found to have the mucosa firmly adherent to the retropubic area when they underwent a subsequent procedure. Some physicians prefer not to cover the myectomized area, assuming that the procedure will reduce overall compliance.<sup>54</sup> After the procedure, a catheter is left in place for 2-7 days. After removal of the catheter, the patient is instructed to do timed voiding, and post-void residuals are checked. Patients who are unable to void are instructed to perform clean intermittent catheterization (CIC) every 3 hours during the day and every 4 hours at night.

Satisfactory results have been reported when autoaugmentation was performed laparoscopically. However, only a limited number of patients have undergone the procedure.<sup>57-59</sup> The operating time for laparoscopic autoaugmentation was reported to be less than 90 min. The hospital stay was brief and postoperative discomfort was minor. Moreover, the laparoscopic approach should not complicate or preclude subsequent enterocystoplasty if it is necessary.



**Figure 20.4** Detrusor myomectomy.  
(Reproduced with permission from  
Leng et al<sup>56</sup>.)

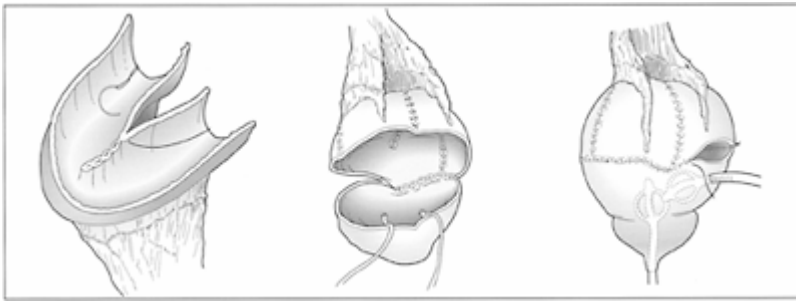
Autoaugmentation may be appropriate for patients with moderately reduced bladder capacity in need of a bladder augmentation to no more than 50% of the original volume. The reported success rates of the procedure reach 80%.<sup>54,55</sup> Kennelly et al reported an overall success rate of 63%, with a 70% success rate for patients with idiopathic instability and a 50% success rate for those with neuropathic instability.<sup>60</sup> These results are inferior to those obtained by enterocystoplasty; however, the morbidity and complication rates also are lower. Complications reported after autoaugmentation are urinary retention and bladder perforation. Urinary retention requiring CIC is observed in fewer than 15% of patients with no underlying urologic deficit.<sup>60</sup> The risk for bladder perforation is higher in patients who require CIC, especially in the early post-operative period.

#### *Enterocystoplasty*

The favorite, and still most commonly used technique for surgically increasing bladder capacity and compliance, is enterocystoplasty, which was introduced by Goodwin in 1958 (Figure 20.5).<sup>61</sup> The goal of enterocystoplasty is to create a reservoir that will maintain low pressure and prevent upper urinary tract deterioration. The lowpressure compliant system buffers the increase in intravesical pressure secondary to uninhibited contractions and ameliorates the sensation of urgency. Vesicoureteral reflux and bladder outlet incompetence may be treated concomitantly. The augmented bladder should hold sufficient volume to be comfortable for at least 4 hours, and at the same time should allow a volume that will enable adequate drainage of the bladder. The augmentation causes the bladder to be spherical in shape so that the volume is determined by its radius, according to the formula  $V = R^3$ . This formula can be employed when calculating the additional volume that is needed for enlarging the bladder and the length of bowel that is required.<sup>62</sup> Various segments of bowel may be used for enterocystoplasty. Each segment of bowel is associated with its own advantages and disadvantages. No matter which segment of bowel is chosen for the enterocystoplasty, several key points should be noted

1. the chosen segment of bowel needs to be detubularized
2. no permanent sutures should be applied to the intraluminal surface of the augment
3. the chosen segment of bowel needs to have sufficient mesentery to reach the true pelvis and be sewn to the bladder without tension<sup>63,64</sup>
4. when the procedure is concluded, a cystostomy tube should be left through the wall of the native bladder and a drain should be left near the anastomotic site.

Various bowel segments have been utilized for augmentation cystoplasty. When ileum is chosen, a segment 15 cm proximal to the ileocecal valve is isolated. The total segment needs to be 20–40 cm long and may be formed into a U-shaped patch after it is detubularized. If a larger augmentation is needed, the patch can be formed into an S- or W-shaped patch. The procedure of enterocystoplasty can be performed laparoscopically. In 1995 Docimo et al performed a laparoscopic gastrocystoplasty in a 17-year-old girl with sacral agenesis.<sup>65</sup> Later reports described use of various segments such as ileum, sigmoid, and right colon.<sup>66</sup> The procedure is an attractive alternative to open enterocystoplasty.



**Figure 20.5** Augmentation enterocystoplasty. (Reproduced with permission from Russell S Jr. Bladder surgery. In: Glenn JF, Boyce WH, ed. Urologic surgery. Second edition. Maryland: Harper & Row Publishers, 1975:300–315.

Cecocystoplasties have been performed since the early 1950s. In the last decade they were replaced by either ileocystoplasty or ileocecocystoplasty. In ileocecocystoplasty a segment of ileum and cecum of equivalent length are mobilized and transected. After detubularization through the ileocecal valve, the bowel is anastomosed to itself and then as a patch on the bivalved bladder. In the Mainz ileocecocystoplasty, a segment of ileum twice the length of the cecum is isolated and anastomosed, first to itself in a U-shape and then to the cecum to create a bigger patch. If needed, a tubularized segment of ileum may be kept as a chimney for subsequent reanastomosis of the ureters.

Sigmoid cystoplasty is employed most often when the mesentery of the small bowel is too short and makes anastomosis to the bivalved bladder impossible. A 15–20 cm length

of sigmoid colon is mobilized and resected. The sigmoid is opened on its antimesenteric side and is formed to either a U-shape or an S-shape. Another technique is to close the two ends of the resected sigmoid and to open the antimesenteric side and then anastomose it to the bivalved bladder.<sup>67</sup>

Two techniques are available for performing gastrocystoplasty. The first is to use the antrum with the blood supply of the left gastroepiploic artery. The gastric pedicle is passed through a window in the transverse mesocolon and mesentery of the distal ileum. The stomach is reanastomosed by a Billroth I gastroduodenostomy. The second technique is to use the gastric body, which is mobilized on either the right or left gastroepiploic vessels. A segment of 10–20 cm of the greater curvature is mobilized and transected in a wedge shape that should not reach the lesser curvature in order to avoid injury to the vagus nerve. The abundance of acid-secreting cells in the stomach used for gastrocystoplasty make it more likely that patients will suffer later with dysuria and other irritative symptoms. Success rates of enterocystoplasty vary considerably and range from 25 to 95%.<sup>63,64,68–72</sup> The wide range reflects the fact that in many series a number of the patients who were treated had interstitial cystitis. These patients, as a rule, gained less from the procedure. Another reason for the wide discrepancy is the inconsistency in defining and measuring success. In some of the studies, success rates vary considerably, depending on the authors' definitions of success and the patients' view of the outcome.<sup>72</sup> The complication rates after enterocystoplasty may be considerable. Flood et al report on 116 patients with early and late complication rates of 22% and 44%, respectively.<sup>73</sup> Among early complications were bowel obstruction (3–10%), urine leakage from the anastomotic line (15%), and wound infection (3–5%). Late complications were diarrhea and bowel dysfunction, vitamin B<sub>12</sub> deficiency, bone demineralization to counteract metabolic acidosis, and an increased risk for adenocarcinoma. Bladder and kidney calculi occur in 8–50%.<sup>73–77</sup> Bladder perforations have been reported in numerous studies, with an incidence of 3–9%.<sup>73,78,79</sup> Some of the perforations were attributed to improper technique or noncompliance with CIC. However, some of the perforations were regarded as 'spontaneous' in patients who were not catheterizing at all. Gastric segments may cause hypokalemic hypochloremic metabolic alkalosis and hematuria-dysuria syndrome. Urinary retention that necessitates CIC occurs in as many as 50% of patients.<sup>69,73,80</sup> The rate of retention correlates with the underlying pathology and the ratio of the bowel's surface area to the entire augmented bladder. All patients need to be informed that they might need to do CIC after the operation and to learn how to perform it prior to the operation.

### **Failure to store: urethra**

Incompetence of the urethra and the sphincteric mechanism may lead to urinary incontinence, which may be continuous or may occur only at times of increased abdominal pressure. Low leak point pressures may occur with or without bladder base mobility, and most patients with sphincteric deficiency have underlying damage to the muscle or innervation of the sphincter. In a subgroup of patients, the sphincteric weakness is secondary to a neurologic deficiency. Among the modalities that exist to



increase outlet resistance are the artificial urinary sphincter (AUS), several sling procedures, and use of periurethral bulking agents.

### *Artificial urinary sphincter*

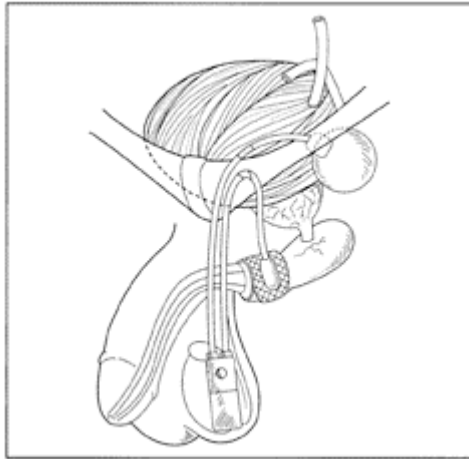
The AUS (American Medical Systems, Minnetonka, Minnesota) was invented about 30 years ago by Brantley Scott. Since the original model was invented, several modifications have been required, and the current model (AMS AS-800) was introduced in 1984. The AUS is a closed system of three components filled with fluid that is transferred between a cuff and reservoir (Figure 20.6). The cuff can be placed around the bulbar urethra or around the bladder neck. The pressure-regulating balloon is placed in the preperitoneal space, and the control pump is placed in the scrotum or the labia major. Since 1972 about 40,000 AUSs have been implanted worldwide. Currently, about 70% of implantations are performed after prostatectomy in patients with stress urinary incontinence.<sup>81</sup>

In the evaluation prior to implantation, the natural history of a patient's underlying disease should be taken into consideration. The patient should have sufficient hand dexterity and cognitive capability to manipulate the AUS. Part of the evaluation is a urodynamic study (UDS). The study should demonstrate a low leak point pressure, bladder capacity of at least 200 ml, no detrusor instability or loss of compliance, and the ability to empty the bladder sufficiently. Contraindications for an AUS implantation are the need for repeated transurethral interventions for problems such as intractable urethral strictures or bladder tumors and/or the presence of distant infected wounds such as pressure ulcers. In men, the cuff is placed at the bulbous urethra. In women and children, the cuff is placed around the bladder neck. The procedure is carried out while the patient is in the lithotomy position. A 3 cm perineal incision is used for placement of the cuff. A 4 cm abdominal incision is made for placement of the balloon reservoir and scrotal pump unless a blind insertion is performed to position the reservoir. All the tubing and connections are manipulated through an abdominal incision. At the end of the procedure, the device is left deactivated for 4–6 weeks. The patient can be discharged on the first postoperative day. There have been various reports in the literature about the durability of the device and patient satisfaction. The overall reoperation rate for the device is 16–25%.<sup>81,82</sup> About 7.5% of revisions occur because of mechanical malfunction of the device, mainly cuff leaks, pump malfunction, reservoir leak, and tubing kinks or leakage. Nonmechanical problems comprise about 12% of all revisions, including urethral atrophy, cuff erosion, infection, pump malposition, and iatrogenic damage to the device. Revision is not possible in 4% of patients. More than 80% of patients who require an AUS will achieve a continence level that will require the use of 1 pad a day at most. Several studies have reported improved quality of life after AUS placement, with 88% of the patients content with the device and 85% who would recommend it to a friend.<sup>83,84</sup>

### *Sling procedures*

Sling procedures were introduced more than 90 years ago. The procedure was offered initially for women with severe urethral incompetence but was scarcely used because of a high complication rate. The initial complications were urinary retention, de-novo detrusor instability, and urethral erosion, particularly when synthetic sling materials were used.

Probably most complications were secondary to placing too much tension on the sling in an



**Figure 20.6** Artificial urinary sphincter. (Reproduced with permission from Goldwasser B, Ramon J. *Prosthetics for urinary incontinence*. In: Webster G, Kirby R, King L, Goldwasser B, ed. *Reconstructive urology* (Vol. 2). Oxford: Blackwell Scientific Publications, 1993:805–16.

attempt to compress the urethra.<sup>85,86</sup> The popularity of the procedure rose after reports by McGuire and Lytton of reasonable cure rates and low complication rates.<sup>87</sup> Over the last two decades the procedure achieved results comparable to those with retropubic suspensions and was offered not only to patients with intrinsic sphincter deficiency but also to patients with all types of incontinence.

The increased popularity of the procedure brought the emergence of novel techniques to reduce the morbidity and invasiveness of the procedure. The procedure initially required abdominal and vaginal incisions, but now there are several new techniques for performing the procedure through a vaginal approach or with a very small abdominal incision. The bone anchoring sling was introduced by Leach in 1988,<sup>88</sup> in a procedure that initially comprised a transvaginal and suprapubic approach. Madjar et al introduced an entirely transvaginal approach for cystourethropexy.<sup>89</sup> Through an anterior vaginal incision, battery-operated drill anchors (titanium screws) connect Prolene sutures into the undersurface of the pubic bone. Two screws are inserted lateral to the urethra. The sling material is attached to the Prolene sutures with no tension. In order to avoid the harvesting of autologous fascia, several other materials such as freeze-dried cadaveric

fascia, xenograft material, or synthetic materials are used. The transvaginal approach results in earlier ambulation and minimal need for narcotics postoperatively. The success rate for boneanchored slings is about 82%.<sup>90</sup> Although there have been some reports of high failure rates using the bone anchored slings, the general impression is that failures are related to the sling material used and not to the anchoring device.<sup>91</sup>

Ulmsten introduced tension-free vaginal tape (TVT; Gynecare, Ethicon, Neuilly, France) in 1996.<sup>92</sup> This procedure can be performed under local anesthesia in an outpatient setting, and involves a 2 cm incision in the vaginal anterior wall over the midurethra and two stab incisions in the suprapubic area. Two trocar needles passed from the vaginal incision upwards toward the suprapubic area position the Prolene tape at the midurethra. Tension adjustment can be calibrated in the operating room until leakage stops when the patient is straining or coughing. No fixation of the tape is required. In most cases the urethral catheter can be withdrawn on the first postoperative day. Short-term efficacy of the procedure was reported, with a success rate of 85–90%.<sup>93,94</sup> Jeffry et al reported an objective success rate of 89.3% and subjective cure rate of 66%.<sup>95</sup> Ulmsten, in his initial study in 1996, and in a later series, reported no significant perioperative complications. Urinary retention of 2–12 days occurred in 10% of patients. Often, investigators reported less-favorable results such as intraoperative bleeding (17%), voiding difficulties (17–27%), bladder perforations (17%), and vascular injuries.<sup>96,97</sup>

Utilizing the same principal of tension-free tape, American Medical Systems (Minnetonka, Minnesota) has introduced the SPARC<sup>TM</sup> system with positioning of the Prolene tape at the midurethra using an antegrade approach, passing the needles from the suprapubic area toward the anterior vaginal wall.

Jorion introduced sling procedures in men in 1997.<sup>98</sup> In Jorion's group a rectus muscle fascial sling was positioned during the radical prostatectomy, resulting in superior continence rates in a small group of men. Schaeffer et al described a suprapubic approach for positioning a sling made of Cortex to treat a group of patients with post-prostatectomy incontinence with satisfactory continence rates of 56%.<sup>99</sup>

Bone-anchored slings to treat incontinent men were introduced in 2001.<sup>100</sup> A gelatin-coated polyethylene terephthalate trapezoid-shaped sling was positioned against the bulbous urethra. Initial success rates were over 85%. Other reports with longer follow-up show a success rate of 75%.<sup>101</sup> Complications secondary to bone-anchored slings include infection and pain. Osteomyelitis, the most worrisome complication, secondary to bone-anchored procedures, is exceedingly rare. There are reports of anchors that had to be removed secondary to localized pain, prolonged wound healing, and excessive discharge.<sup>102</sup> The incidence of urinary retention is minimal and there is a small incidence of de-novo detrusor instability.<sup>103</sup>

### *Peri urethra I bulking agents*

The mechanism of action of bulking agents is to increase the urethra's passive closure pressure by better coaptation of the mucosa. Selection of patients appears crucial to the outcome of periurethral injection with bulking agents. The ideal candidate for this procedure is one who has good anatomic support, a normally compliant and stable bladder, and a urethra with intrinsic sphincter deficiency and a low leak point pressure. Other subsets of patients who may benefit from the procedure are (1) patients with higher

leak point pressures and minimal hypermobility and (2) elderly women with bladder base mobility who are less active and are a poor surgical risk for other interventions.

Periurethral bulking agents have been in routine use for more than a decade. The desirable injectable material should be biocompatible, non-immunogenic, and hypoallergenic. The material should retain its bulking characteristics for an extended period of time and neither degrade nor migrate. The material should be easily targeted and injected. As yet, there is no bulking agent that meets all of these criteria, and the search for the ideal bulking agent continues. Most agents provide satisfactory results only after repeated treatments. Currently, there is no method to predict how many injections a given patient will need. The position, volume, and the operator's impression of tissue coaptation have not been correlated with clinical outcome, and the optimal timing between injections has not been determined. The outcomes for procedures using bulking agents vary considerably, depending on the method of assessment. Currently, there is no standardized regimen for evaluating the procedural result. The definition of cure may vary from absolute dryness to acceptable social comfort. Any assessment of results should include the information about the patient's selection, the number of injections required, volume of each injection, and the timing of assessment since the last treatment.

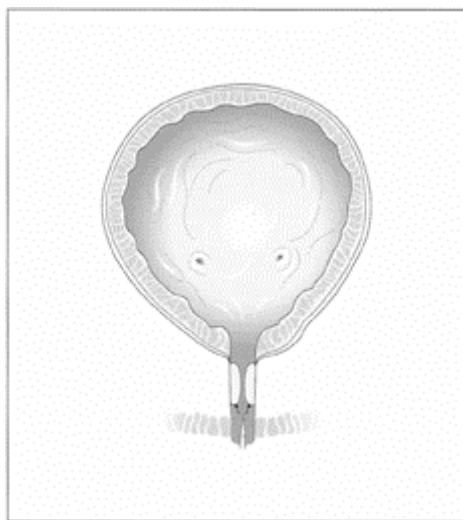
Currently, the most commonly used injectable is a sterile bovine dermal collagen (Contigen™) that is cross-linked with glutaraldehyde and is dispersed in phosphatebuffered saline that comprises about 65% of the total injectable volume. The FDA approved the material in 1993 for male and female intrinsic sphincteric deficiency (ISD). This collagen is both biocompatible and biodegradable. The glutaraldehyde cross-linking reduces the antigenicity of the material and makes it less degradable by collagenase. In the early period after collagen injection, the buffered saline vehicle is reabsorbed. The collagen begins to degrade in approximately 3 months after the injection and is completely degraded within a period of about 10–20 months.<sup>104</sup> There are no reports of particle migration. The material achieves part of its bulking effect because of neovascularization and fibroblast ingrowth into the implant. Collagen may be injected either transurethrally, through a cystoscope, or periurethrally, by using a spinal needle inserted percutaneously, with simultaneous viewing through a cystoscope for material positioning and effect (Figure 20.7).<sup>105,106</sup> Another technique available is percutaneous periurethral injection with placement of the material monitored by ultrasonography.<sup>107</sup> The optimal depth of collagen placement appears to be into the superficial urethral muscle adjacent to the submucosa.<sup>108</sup> No matter which technique is used, precise placement of the material is of paramount importance.

Injection of bulking agents may be done as an office procedure. The patient is placed in the lithotomy position. The introitus is anesthetized with 20% topical benzocaine and the urethra is anesthetized with 2% lidocaine jelly. A local injection of 1% lidocaine is given periurethrally at the 3 and 9 o'clock positions with a total volume of 2–4 ml on each side. When the periurethral approach is used, urethroscopy is performed with a 0° or 30° lens. A 20F spinal needle with the obturator in place is positioned periurethrally at the 4 or 8 o'clock position, with the bevel of the needle directed towards the lumen. The needle's tip can be seen below the mucosa, bulging toward the urethral lumen. Before the injection, the cystoscope is aimed so that the bladder neck and bladder can be observed simultaneously. During injection, swelling is visible, protruding toward the lumen. If, during injection, the mucosal surface becomes blanched or the collagen is visible under

the mucosal surface, then the material has been injected too superficially and the needle should be repositioned. After occlusion of about 50% of the lumen, the needle is withdrawn and reinserted on the opposite side. Following the injection of the second side, the bladder neck may resemble the appearance of two 'kissing' lateral prostatic lobes. Correlation of the success rate with the position and volume of collagen injected has been examined.<sup>109</sup> Most patients require 2–5 injection sessions in order to attain satisfactory results, and subsequent injections are needed to maintain the continence achieved. The improved/cure rate is 70–90%, whereas the actual cure rate is about 40–60% at best.

Complications associated with collagen injections include de-novo urgency (13%); urinary retention, which is brief and resolves by itself in 2%; urinary tract infection (1–4%); and hematuria (5%). An early hypersensitivity reaction may occur in up to 3.5% of patients and delayed hypersensitivity reaction may occur in about 1%.<sup>109–111</sup> Another less common complication is the formation of a sterile abscess.<sup>112</sup>

Pyrolytic zirconium oxide beads (Durasphere), coated with carbon in the size range of 200–500  $\mu\text{m}$ , were approved by the FDA in September 1999. The Durasphere particles are suspended in a water-based beta-glucan vehicle. The material is intended for injection submucosally at the bladder neck using an 18-gauge needle through



**Figure 20.7** Transurethral collagen injection.

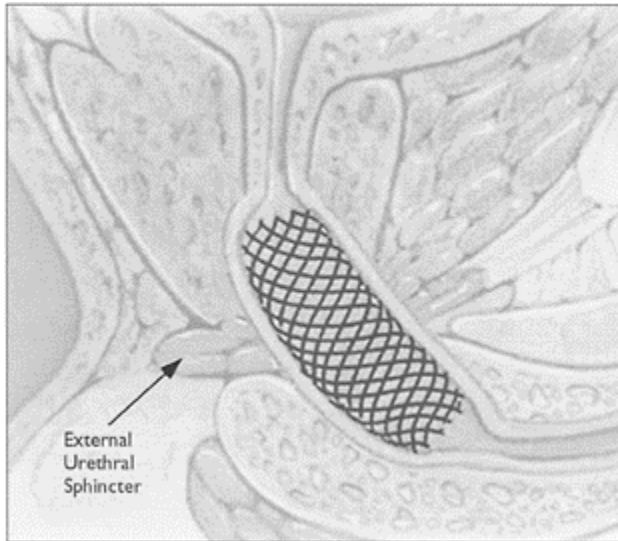
the cystoscope. More recently, a periurethral needle has been introduced. As yet, there is very limited literature concerning this injectable agent. A randomized, multicenter, double-blinded study conducted for FDA approval comparing collagen to Durasphere showed similar improvement in continence.<sup>113</sup> In that study adverse reactions attributed to Durasphere treatment were acute retention (<7 days' duration) (16%), dysuria (12%), urinary tract infection (9%), and irritative symptoms (15%). Because Durasphere is more viscous than collagen, its injection is technically more demanding. Among numerous

other injectable materials that are currently being evaluated in clinical studies are human collagen, autologous chondrocytes, hyaluronic acid and dextranomer microspheres, ethylene vinyl alcohol copolymers and myoblast injection. Some of these materials have provided encouraging results in preliminary studies and will enter the market in the near future.

### **Failure to empty: urethra**

Patients with spinal cord lesions caused by trauma or degenerative conditions such as multiple sclerosis may have detrusor-external sphincter dyssynergia (DESD). Many of these patients have elevated voiding pressure and poor bladder emptying with elevated residual volume. The long-term complication rate for these patients is 50%. Complications include sepsis, vesicoureteral reflux, nephrolithiasis, and renal function deterioration.<sup>114–116</sup> Treatment options for these patients include pharmacologic therapy, intermittent catheterization, indwelling catheters, urethral stents, external sphincterotomy, botulinum injections to the external sphincter, and urinary diversion. All of these management options reduce the intravesical pressure and thus protect the upper urinary tract. Some of these surgical options, excluding diversion, render the patient incontinent and thus the patient will require an external condom catheter or other means of protection.

UroLume (American Medical Systems, Minnetonka, Minnesota) is a 1.5–3 cm stent made of nonmagnetic superalloy woven into tubular mesh. The stent can be inserted using a 21F insertion tool and deployed in the membranous urethra across the external urethral sphincter (Figure 20.8). When deployed, the UroLume stent opens up to the diameter of 42F with radial force that keeps the external sphincter permanently open. Urothelial cells infiltrate the interstices and cover the stent completely. Chancellor et al conducted a multicenter trial of 160 spinal cord patients with DESD who had a UroLume stent placed across the external sphincter.<sup>117</sup> In a



**Figure 20.8** UroLume stent for detrusor-external sphincter dyssynergia. Urolume<sup>®</sup> Endoprosthesis. Courtesy of American Medical Systems, Inc. Minnetonka, Minnesota.  
<http://www.americanmedicalsyste.ms.com/>

5-year follow-up study the patients maintained a decrease in voiding pressure and lowered their post-void residuals (PVR) with no adverse effect on bladder capacity or renal function. Stenosis and encrustations of the stent occurred in about 3.1 and 6% of patients, respectively. About 27% of the patients required more than one stent to be placed across the sphincter. In 22.7% of patients migration of the stent occurred during the first postoperative year. Following sphincterotomy and transurethral prostatectomy, there seems to be a higher risk for stent migration. Several complications have been reported with the UroLume stent, such as stent migration, stent occlusion because of tissue ingrowth, and penile discomfort.<sup>118,119</sup> In case of stent migration, the multicenter study group recommends that the physician resect the overlying urothelium, push the stent into the bladder, and extract it through the outer sheath of a cystoscope. Gajewski et al reported the use of this technique when describing difficulty extracting the stent from 2 patients.<sup>120</sup>

*Sphincterotomy*

The primary indication for sphincterotomy is DESD that has failed conservative treatment. The procedure involves an incision from the verumontanum along the entire length of the membranous urethra. The incision should be made at the 12 o'clock position and should involve the entire muscle width. Success rates are 70–90%.<sup>120–122</sup> In most cases early failures are caused by inadequate incision or an acontractile detrusor. Common complications are hemorrhage (5–20%), erectile dysfunction, and urinary extravasation.

*Botulinum A toxin*

As mentioned previously, BTX selectively blocks the release of acetylcholine from nerve endings and blocks neural transmission. When injected directly into the muscle, BTX binds to nerve terminals and has a prolonged and sustained effect.<sup>27</sup> The toxin can be injected endoscopically into the external sphincter to temporarily eliminate its activity. The effect lasts 3–9 months. There have been few reports regarding this technique, with no reports of adverse effects or allergic reactions. The procedure provides a therapeutic option for patients who desire a reversible form of therapy.<sup>123–125</sup>

*Pudenda I nerve blocks*

Motor control of the external sphincter is supplied through the pudendal nerve that emerges from the S2–S4 roots and descends through Alcock's canal. As the nerve exits from the canal, medial to the ischial tuberosity, it can be blocked temporarily by lidocaine 1% or permanently by phenol or surgical removal. After a good response to the lidocaine injection, evident in anal sphincter tone, perineal sensation, and reduced PVR, a permanent approach may be selected. In most cases only the medial branch of the pudendal nerve is resected unilaterally. In a few reports, durable success rates of about 78% were reported.<sup>126,127</sup> Because of the technical difficulty in approaching the pudendal nerve, this form of neurectomy is seldom used to manage sphincteric dysfunction.

**Failure to empty: bladder**

Incontinence may ensue because of detrusor hypocontractility or areflexia and the inability of the detrusor to generate sufficient force to expel the urine. Testing often demonstrates delayed sensation with large capacity and a very compliant bladder. During the voiding phase no detrusor contraction is evident when the patient tries to empty his bladder. The treatment options for managing the areflexic bladder are very limited. Jonas et al<sup>128</sup> evaluated 17 patients with idiopathic urinary retention. Most had voiding dysfunction secondary to nonrelaxation of the external urethral sphincter. Of this group, approximately 50% showed significant improvement in response to the temporary sacral nerve stimulator. All patients who showed a favorable response were divided into a study and a control group. Of the patients treated with implants, 69% eliminated catheterization



at 6 months and an additional 14% had a 50% or greater reduction in catheter volume per catheterization. Therefore, successful results were achieved in 83% of the implant group with retention compared with 9% of the control group at 6 months. Temporary inactivation of sacral nerve stimulation therapy resulted in a significant increase in residual volumes ( $p < 0.0001$ ) and effectiveness of sacral nerve stimulation was sustained through 18 months after the implantation.<sup>128</sup>

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## 21

# Minimally invasive approaches to female urinary incontinence and pelvic floor dysfunction

Richard T Kershen and Rodney A Appell

### Introduction

Increased public awareness of effective therapies for urinary incontinence and voiding dysfunction has led more patients to seek treatment and ultimately undergo surgery. In parallel with recent additions to the pharmaceutical arsenal for the treatment of these disorders, the surgical armamentarium has rapidly expanded, with the addition of novel, minimally invasive techniques. Classical retropubic suspensions and autologous pubovaginal slings for stress urinary incontinence (SUI) have been modified through the use of transvaginal suturing devices and newer sling materials, or supplanted with injectables and transvaginal midurethral slings. Alternatives to surgical bladder augmentation have been developed to alleviate the debilitating symptoms of refractory overactive bladder while limiting the necessity of enteric interposition into the urinary tract. When bladder augmentation does become necessary, the procedure may now be performed laparoscopically. These techniques have been embraced by the urologic community with the hope of decreasing post-operative pain, length of hospital stay, and time off from work, while maintaining equivalent efficacy and morbidity. In some cases these goals have been achieved, while in others, clear benefit has yet to be established. In this chapter we will review both established and novel minimally invasive approaches directed at the treatment of urinary incontinence and pelvic floor dysfunction.

### MINIMALLY INVASIVE APPROACHES FOR THE TREATMENT OF INCONTINENCE

#### Diagnosis and evaluation

*Is the incontinence stress, urge or mixed?*

As always, a careful history is essential to properly assess the nature and severity of a given patient's symptoms. Does the incontinence occur only with stress (Valsalva) maneuvers such as coughing, sneezing, laughing, or physical exercise or does it also occur with minimal activity or while supine? Is the patient using protective pads? If so, how many are used during the course of an average day? Is the patient experiencing significant urinary frequency (voiding more than every 3 hours) and nocturia? Is the

problem related to isolated urge incontinence that occurs when she simply cannot reach the bathroom in time?

Often patients will have mixed symptoms, and knowing which symptoms are particularly bothersome is important in developing a treatment plan. Symptom scores such as the Urogenital Distress Inventory (UDI), Incontinence Impact Questionnaire (IIQ), or the American Urological Association (AUA) Symptom Score may be helpful in this regard. Symptoms such as hesitancy, poor urinary stream, intermittency, straining to void, and sensation of incomplete voiding suggest the presence of obstruction and may indicate the presence of occult neurogenic or myogenic bladder dysfunction or anatomic obstruction resulting from pelvic prolapse or previous operations. The presence of associated difficulties with defecation should also be determined. A thorough medical history should be elicited to record previous operations, including hysterectomy, prolapse repair, or an anti-incontinence procedure, as well as medical comorbidities that may affect lower urinary tract function such as diabetes, multiple sclerosis, cerebrovascular disease or intervertebral disc disease. A list of the patient's current medications should be obtained, because many can affect lower urinary tract function and may alter surgical decision making. Caffeine, tobacco, and alcohol intake levels should also be determined as each may affect voiding frequency. We find that a voiding diary which records fluid intake and urinary output as well as leakage episodes over a 2–3-day period, may prove invaluable in guiding proper diagnosis and therapy.

A directed urogynecologic examination is performed to determine the status of pelvic floor integrity and search for anatomic causes of incontinence. We begin our examination with a visual inspection of the external genitalia:

- Is there gross prolapse through the introitus?
- Are there signs of estrogen deficiency such as urethral caruncle or genital atrophy?
- Are the labia excoriated from chronic exposure to urine indicative of severe incontinence?

We then proceed with a cotton-tip applicator test to determine the degree of urethral hypermobility. A cotton-tip applicator is inserted in the urethra to the level of the bladder neck. The resting angle of the applicator relative to the horizontal plane is then determined. A negative resting angle after a bladder suspension may indicate a hypersuspended urethra. The patient then performs a maximal Valsalva maneuver and the change in resting angle of the applicator is observed. A change in the angle of more than 30° indicates significant urethral hypermobility. Next, a post-void residual is determined to measure bladder emptying and to rule out overflow incontinence. A halfblade speculum examination is then performed to look for the presence of associated pelvic prolapse. The anterior vaginal wall should be examined for the presence of cystocele, the posterior vaginal wall for the presence of rectocele, and the vaginal apex for presence of enterocele and/or uterine or vault prolapse.

Although patients who have pure urgency incontinence may benefit from an empiric course of anticholinergic therapy without further evaluation, we perform urodynamic testing on all patients who come for evaluation and treatment of stress incontinence. We believe this is essential in directing us toward the proper line of surgical therapy. Although an in-depth description of urodynamic testing techniques is beyond the scope of this chapter, a brief synopsis of our basic evaluation is appropriate. We perform



videourodynamic testing, integrating live fluoroscopic images of the bladder and outlet with real-time intra-abdominal and intravesical pressure monitoring.

Electromyography (EMG) of the pelvic floor is also employed when neurologic injury or pelvic floor spasticity is suspected. Calculated detrusor pressure is used to reflect true bladder function. Each study involves evaluation of both the storage and emptying phases of micturition as well as determination of outlet competency via Valsalva leak point pressure (VLPP) measurement. We typically fill the bladder at a medium fill rate of 60–80 ml/min. During the filling phase of the study, we monitor the tracing for evidence of motor detrusor overactivity and note the patient's varying sensations of fullness and urgency. After 200, 250, and 300 ml of filling, the VLPP is determined under fluoroscopic guidance. Fluoroscopy will also reveal the degree of urethral hypermobility during Valsalva as well as the presence of a central or lateral defect cystocele. After a patient's maximum cystometric capacity is reached, she is asked to void, during which time the maximum flow rate and detrusor pressure at maximum flow are determined to evaluate the voiding mechanism. Finally, the post-void residual volume is measured. Using this evaluation, we can almost always determine the functional cause of a patient's symptoms. The relative contributions of urethral hypermobility and intrinsic sphincteric deficiency (ISD) to the etiology of stress incontinence can be assessed as well as the presence of primary bladder dysfunction. We uniformly base our treatment plan upon an integration of the patient's symptoms and clinical findings with the urodynamic testing results.

## **Treatment of stress urinary incontinence**

### *Nonsurgical treatment options*

An effective pharmaceutical agent for the treatment of SUI has yet to be developed. Alpha-adrenergic agonists such as ephedrine and pseudoephedrine, implemented in the past to augment proximal urethral function, have met with marginal clinical success and significant side-effects.<sup>1,2</sup> Estrogens have been utilized in the hope of improving intrinsic sphincteric smooth muscle function, but in randomized trials they have been shown to be ineffective.<sup>3,4</sup> Other noninvasive therapies, including Kegel exercises, biofeedback, and pulsed electromagnetic energy to the pelvic floor, directed at enhancing volitional control over external sphincteric function have been shown to have some benefit over no treatment at all or placebo, but high-quality, randomized, long-term trials are lacking.<sup>5–7</sup>

### *Minimally invasive surgical therapy*

#### **Choice of procedure: Which one for which patient?**

Once the decision has been made to proceed with a surgical endeavor, how should one determine which procedure to use? A variety of viable alternatives are available. Our choice of procedure is based on the integration of a number of factors, including age of the patient, clinical history, and urodynamic results. Of course, patient preference plays an important role as well. Injectables are an excellent choice for patients with pure ISD

and minimal urethral hypermobility who want to completely avoid an incision. Patients need to understand, however, that currently, to achieve their desired goal, they may need to undergo several injections and the effects may not be long lasting, requiring retreatment within 2 years. For the patient with significant hypermobility but adequate intrinsic urethral function with VLPP  $>70$  cmH<sub>2</sub>O, a transvaginal midurethral sling or in-situ vaginal wall sling is preferred. For patients with severe ISD and VLPP  $< 70$  and age  $<65$  years old, we favor an autologous rectus fascia pubovaginal sling, which, although more invasive, has the longest successful outcome data. For older patients, a bone-anchored pubovaginal sling using donor material is preferred. In the presence of associated pelvic prolapse, a bone-anchored sling allows the entire operation to be performed transvaginally.

### *Injectables*

Since the Food and Drug Administration (FDA) approval of glutaraldehyde cross-linked (GAX) bovine collagen in 1993, injectables have gained acceptance for the treatment of female SUI. The goal of endoscopic injection therapy is to provide a minimally invasive, effective, and safe alternative to open surgical treatment. Although the ideal injectable bulking agent has yet to be developed, currently available agents have met most of these criteria. Injection therapy is clearly the least invasive of all surgical therapies available for the treatment of incontinence. Endoscopic treatment may be performed with the patient under local anesthetic without sedation, and does not preclude future, more invasive surgical management. It has been and continues to be the best treatment alternative for elderly patients unfit for major surgery. In addition, it can be used as a salvage therapy in patients who have failed previous invasive surgical procedures.

The mechanism by which injectable bulking agents improve continence has not been completely elucidated. It appears that provision of additional submucosal bulk to the proximal urethra results in mucosal coaptation and thus increases urethral closure pressure and resistance to the passive outflow of urine.<sup>8</sup> After successful injection, there is cephalad elongation of the functional urethral length, resulting in an increase in the efficiency of pressure transmission to the most proximal one-quarter of the urethra, likely resisting bladder neck opening during stress.<sup>9</sup> An increase in VLPP has been demonstrated in cured or improved patients after injection therapy.<sup>10-12</sup>

We consider a patient an ideal candidate for injection therapy if she demonstrates SUI due to ISD without significant urethral hypermobility. In this patient group, success rates as high as 95% have been reported.<sup>13</sup> Patients who have urethral hypermobility or type II incontinence may also benefit from treatment, with approximately 60–65% of women reported cured or improved after variable follow-up.<sup>10,14</sup> In all patients a suitable recipient site for injection is an absolute prerequisite for this form of therapy, as dense urethral scarring will preclude entrance into the correct plane and inhibit adequate bleb formation. In addition, the presence of detrusor instability and poor bladder compliance should be detected prior to injection therapy as these conditions will severely limit treatment success.

At present two injectable agents are currently approved for human use in the United States, bovine GAX collagen (Contigen; CR Bard, Inc., Murray Hill, New Jersey) and pyrolytic carbon-coated zirconium beads (Durasphere; Carbon Medical Technologies,

Inc., St Paul, Minnesota). The equipment required for injection depends on which bulk-enhancing agent is injected. The injection can be performed either suburothelially through a cystoscopic needle placed directly through the mucosa (transurethral injection), or periurethrally with a needle inserted percutaneously and positioned in the urethral tissues in the suburothelial space, with the manipulation observed cystourethroscopically.<sup>15</sup> The periurethral approach, although considered more technically challenging, offers the advantage of minimization of intraurethral bleeding and extravasation of the injectable substance. We have found that this is the best approach to injecting Durasphere.

There is certainly a learning curve with any technique chosen, which ultimately results in using less injectable material to attain the desired result of continence. We perform all injections in females in the office setting with the patient under local anesthesia, although additional intravenous sedation in the operating room is a reasonable alternative.

Patients receiving GAX collagen must undergo a skin test 1 month prior to their first injection to exclude allergy to the material. Certain basic tenets should be adhered to with either injection technique. In general, the material should be injected slowly and under direct vision into the proximal urethra. The cystoscope should not be advanced beyond previously injected zones, as this may result in compression or extrusion of the bulking material. At the completion of the procedure, if the patient cannot void, the bladder typically is drained with the gentle passage of a 12 or 14F catheter that is removed immediately.

### **Establishment of local anesthesia**

Local anesthesia is established identically for periurethral or transurethral injection. With the patient in the lithotomy position, local anesthesia of the urethral mucosa and external meatus is accomplished via the transurethral retrograde injection of 2% lidocaine jelly. Anesthesia of the introitus can be accomplished with 20% benzocaine ointment, allowing subsequent painless injection via a 1.5 inch, 25-gauge needle of an additional amount of 1% lidocaine without epinephrine into the periurethral region. A volume of 4 ml delivered to both the 3 and 9 o'clock positions is normally sufficient to achieve complete urethral sensory blockade.

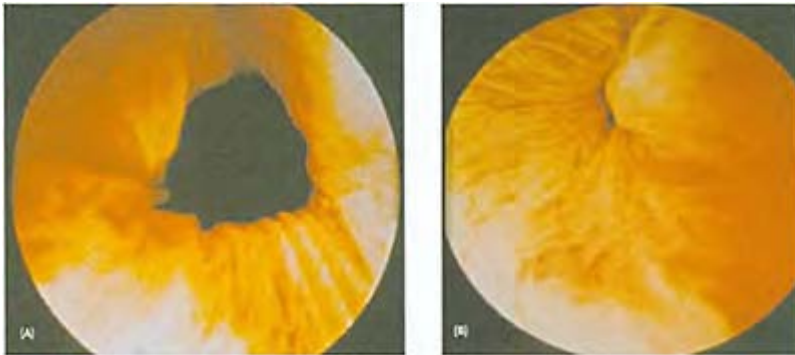
### **Technique of transurethral injection**

A standard 21–24F cystoscope or hysteroscope that can accommodate a 5F working element with a 0, 12, or 30° lens is used to perform cystourethroscopy. The region of injection just distal to the bladder neck is identified and a needle delivery system with or without external sheath is advanced through the working channel. The needle with bevel facing toward the lumen then punctures the mucosa and is advanced proximally into the submucosal space, typically at the 4 or 8 o'clock position. The bulking material is slowly injected until a mucosal bleb of sufficient size is achieved. The process is repeated on the opposite side and at any other site necessary to achieve total mucosal apposition (Figure 21.1). Care must be taken to avoid puncturing the mucosa at previously injected sites as this may result in extrusion of the bulking material.

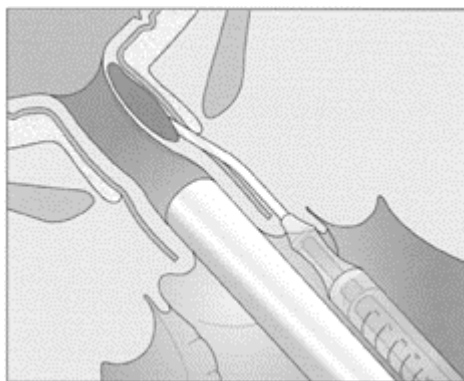
### Technique of periurethral injection

A 20-gauge spinal needle is inserted at the 4 o'clock position and advanced proximally under direct cystoscopic vision until reaching the submucosal space of the urethra, just distal to the bladder neck. The bulking material is then slowly injected with the bevel of the needle facing the lumen until a mucosal bleb is raised to the midline. The procedure is then repeated at the 8 o'clock position until the lumen appears sufficiently occluded, assuming the appearance of obstructing prostatic lobes.

We modify this technique for the injection of Durasphere (Figure 21.2). Using a specially designed bent needle, we perform gentle hydrodissection with normal saline initially under cystoscopic guidance, raising a mucosal bleb, mimicking the desired shape of the implant. The Durasphere implant is then injected with minimal resistance into the potential suburothelial space created by the hydrodissection. The Durasphere implant displaces the normal saline, which is dispelled around the needle tip.



**Figure 21.1** Cystoscopic appearance before and after injection of a bulking agent. (A) Prior to injection, proximal urethral incompetence is readily apparent. (B) After injection of the implant, the lumen should appear occluded, mimicking obstructing prostatic lobes.



**Figure 21.2** ‘Bent needle’ periurethral injection technique of Durasphere in a female patient. The bent needle is advanced into the suburothelial plane towards the bladder neck. Hydrodissection with normal saline is then gently performed, creating a submucosal space. The Durasphere implant is then injected with minimal resistance into the space created.

This technique facilitates precise implant placement, minimizing both extrusion of the material and, ultimately, the amount of implant required for urethral coaptation.

### **Outcomes with injectable therapies**

Studies evaluating the efficacy of collagen for the treatment of female SUI with a minimum of 1 year mean follow-up report cured or improved rates from 26% to 95%. Results of the North American Contigen Study Group of 127 women demonstrated 46% dry and 34% socially continent (patients requiring a single minipad/ day) with 77% remaining dry once continence had been attained.<sup>16</sup> A study with longer follow-up was performed by Corcos and Fournier who followed patients for up to 50 months after the initial injection.<sup>10</sup> They found that efficacy was preserved long-term, with 30% and 40%, respectively, cured or improved. In this group, 33% of patients required more than one injection session to achieve treatment success. The average volume of collagen injected to achieve cure in their cohort was 8.8 ml. As with most injectables to date, a loss of treatment efficacy over time and need for reinjection have been observed with collagen. In fact, 12–40% of patients who achieve initial success will need reinjection within 2 years.

Lightner et al performed the first study evaluating the safety and effectiveness of Durasphere compared with bovine collagen for the treatment of ISD.<sup>17</sup> A total of 355

women with ISD were randomized to receive either Durasphere or bovine collagen. At 12 months follow-up from baseline, patients who received Durasphere were shown to have a mean reduction in pad weight similar to that in patients who received bovine collagen (27.9 g and 26.4 g, respectively). In addition, 66.1% of the patients receiving Durasphere demonstrated an improvement of one or more Stamey continence grades compared with 65.8% of the patients who received bovine collagen. When evaluated at 1 year after the date of the last injection, 80.3% of women who were treated with Durasphere were improved relative to 69.1% of the women who received collagen. The mean number of injections were similar for both groups (Durasphere, 1.69; bovine collagen 1.55), but the total volume of material injected was lower in the Durasphere group (7.55 ml vs 9.58 ml). Unfortunately, a recent study of long-term follow-up (average=24.2 months) in 50 of these patients who received Durasphere found that, subjectively, 86% had experienced leakage since their injections.<sup>18</sup> Seventy-nine percent of the patients who leaked stated that they continued to have multiple incontinent episodes each day. In addition, 38% of patients believed that the injections never made any improvement in their urinary leakage. Durasphere had a transient effect, lasting an average of 7.7 months in 38% of patients. Only 24% of patients thought that the Durasphere had a durable effect and was still working at an average time since last injection of 21.9 months (range 12.1–52.8 months). Overall, 40% of patients subjectively believed that the injections were ‘successful’ and 48% would recommend this form of treatment to a friend. This follow-up study reveals that despite initial enthusiasm for Durasphere as a more durable bulking agent, its long-term results are no better than GAX collagen, with the majority of patients experiencing recurrent or persistent leakage within 8 months after treatment, even after initial apparent success.

### **Complications of injectables**

Regardless of the material, the use of periurethral injections has proven to be safe, eliciting only minor complications. All complications resolve rapidly, and a serious long-term complication from the use of periurethral GAX collagen or Durasphere injections has yet to be reported. Authors have reported de-novo urgency and urinary retention rates at 13% and 2%, respectively.<sup>19</sup> In all cases, urinary retention is short lived as a rule, resolving spontaneously.

Clinical experience with both GAX collagen and Durasphere has demonstrated that the endoscopic correction of female SUI is both possible and effective. It is clear, however, that durability remains a primary concern when implementing this approach to treatment. In the future, as newer technologies are developed and long-term success rates increase, this therapy may possibly become the treatment of choice for SUI.

### *Slings*

In recent years the types of slings available for the treatment of SUI have rapidly increased. Classical autologous pubovaginal slings have been either modified, through the use of donor or synthetic sling materials with bone anchor fixation to the pubis, or supplanted with transvaginal midurethral slings. Knowledge of female pelvic anatomy and physiology has allowed a rethinking of both older and newer procedures, maximizing

potential therapeutic efficacy while minimizing operative time, hospital stay, post-operative pain, and duration of convalescence. We will discuss the advantages and pitfalls of these newer approaches to sling surgery.

### Choice of sling material

Although patient-derived, autologous sling materials such as rectus fascia or fascia lata represent the gold standard for use in pubovaginal sling surgery, off-the-shelf tissue allografts, xenografts, or synthetics, as well as in-situ materials, represent an attractive alternative. A variety of materials are available to choose from, many of which have promising short-term data proving efficacy.

Unfortunately, long-term data are lacking for most of these materials. The major advantage of an off-the-shelf product for use as a sling is that the pubovaginal sling surgery is converted to a minimally invasive procedure. This advantage is also obtained by using autologous vaginal wall as the sling material. When these materials are used, the abdominal incision can be significantly reduced in size or eliminated completely, leading to a marked reduction in postoperative pain experienced by the patient. The largest experience exists with cadaveric fascia lata. There have been reports of early and intermediate-term failures along with excellent intermediate-term data. It appears that the long-term integrity of the material may depend upon where it is harvested and the mechanism by which it is processed (i.e. irradiation vs dehydration).

There has been a concern among physicians that these implants may carry and transmit infectious disease, although, to date, there are no reported cases in the literature. Xenografts such as porcine dermis or bovine pericardium previously used by plastic surgeons have been used with efficacy, but few reports exist in the literature. Polypropylene mesh slings as well as polytetrafluoroethylene (PTFE) have been used effectively by several investigators. Choice of sling material is largely based on the surgeon's personal preference and, until long-term data are available, no material can be objectively considered superior to any other.

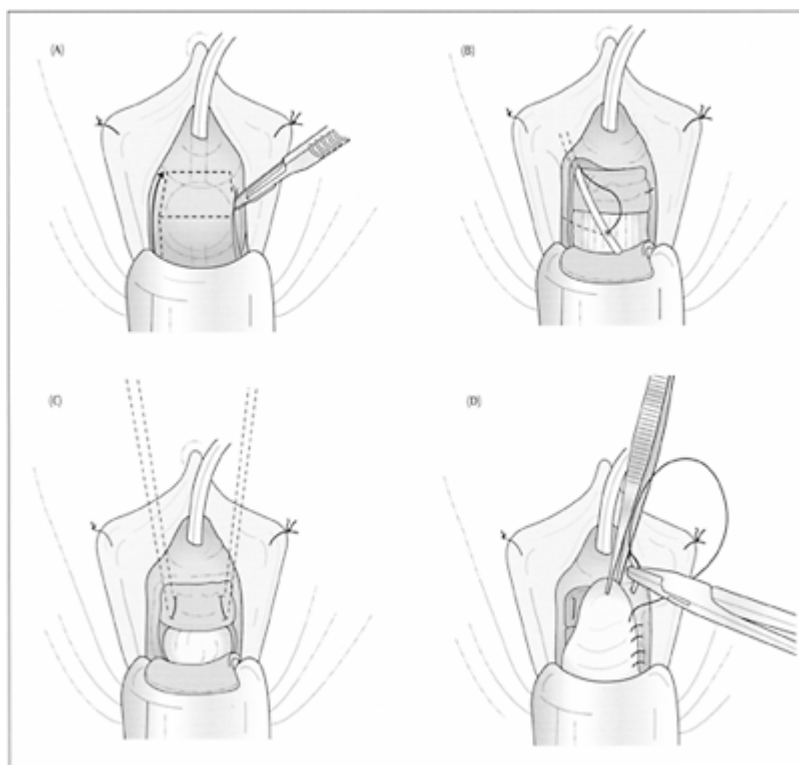
### Stable fixation point transvaginal slings

Failure of now-abandoned, transvaginal needle suspensions has been linked to pull-through of permanent suspension sutures through weakened periurethral and vaginal tissues.<sup>20</sup> Rabbit models have indeed demonstrated this phenomenon, whereby tension applied to sutures affixed to weakened tissues resulted in pull-through.<sup>21</sup> Based on this evidence, it logically follows that sling sutures tied over the rectus muscle, as they commonly are in conventional pubovaginal sling surgery, may saw through sling materials during Valsalva maneuver because they are not stabilized on a solid structure. Sling suture fixation to the pubic bone will eliminate this possibility by provision of a solid fixation point for suspending sutures. A fixed point of attachment will prevent suture movement thus prevent suture pull-through.<sup>22</sup> during Valsalva maneuver or abdominal contraction and

**In-situ vaginal wall sling affixed to the pubic bone.** The in-situ vaginal wall sling was first introduced by Raz et al in 1989.<sup>23</sup> This technique, by utilizing in-situ vaginal wall over the bladder neck and proximal urethra as the sling material, eliminates the need for

fascial harvest and renders the procedure less invasive. In addition, the use of autologous vaginal tissue avoids the potential complications of erosion or infection associated with synthetic material. Vasavada et al first described a modified technique of in-situ vaginal wall sling placement that implemented the use of bone anchors with preservation of the endopelvic fascia.<sup>24</sup> With this technique, dissection around the bladder neck and proximal urethra is minimized, respecting anatomic integrity and reducing the risk of neurovascular injury or future prolapse. Although we originally used suprapubic bone anchors for suture fixation, we currently favor open suture fixation to the pubic bone that requires a minimal (3 cm) suprapubic incision. This attains a stable point of suture fixation while virtually eliminating the potential for osteomyelitis, as discussed later. Using this technique, we have achieved cure rates better than 90% in patients with VLPP  $>50$  cmH<sub>2</sub>O with mean follow-up of 19 months or more.<sup>25</sup>

*In-situ vaginal wall sling—surgical technique:* The procedure begins by formation of the in-situ sling. A block 'A' incision is made in the anterior vaginal wall with the island of the 'A' serving as the sling, and the vaginal wall between the legs of the 'A' serving as a flap of tissue that will later cover the sling at closure (Figure 21.3A) Dissection is carried out to expose the pubocervical fascia and mobilize



**Figure 21.3** In situ vaginal wall sling.  
(A) A 'block A' incision is made in the



anterior vaginal wall with the island of the W serving as the sling and the vaginal wall between the legs of the 'A' serving as a flap to cover the sling defect. (B) A suture passer delivers a Prolene suture to the vaginal incision from behind the pubis. (C) The vaginal sling sutures are then redelivered to the suprapubic incision using the originally placed suture passers. (D) The vaginal wall incision is closed by covering the lower part of the W incision into an inverted 'U' incision.

the vaginal wall lateral to the sling. A 3 cm transverse suprapubic incision is then made and developed to the level of the pubic symphysis. Zero Prolene sutures are then secured in a figure-of-eight fashion to the bilateral pubic tubercles and delivered to the vaginal incision using two suture passers (Figure 21.3B). After cystoscopy confirms bladder integrity, a free needle is then used to secure each suture to each side of the in-situ sling using a simple horizontal mattress technique. The sutures are then redelivered to the suprapubic incision using the originally placed suture passers (Figure 21.3C). The vaginal wall is then closed in a running fashion with a No. 2 Vicryl suture, converting the 'A' incision into an inverted 'U' incision (Figure 21.3). The sling sutures are tied down over a suture spacer bilaterally to set a fixed sling tension, completing the procedure.

**Transvaginally bone-anchored pubovaginal slings.** Newer bone-anchoring techniques have enabled pubovaginal sling surgery to be performed completely by the vaginal route, eliminating the necessity of an abdominal incision. Bone anchors may be inserted without perforation of the endopelvic fascia as previously described with the in-situ vaginal wall sling. This may reduce the incidence of postoperative voiding dysfunction and prolapse. Bone anchors may also be implemented for simultaneous combined pubovaginal sling and cystocele repair, as described by Kobashi et al.<sup>26</sup>

*Transvaginally bone-anchored pubovaginal slings—surgical technique:* When placing bone anchors, it is our preference to use broad-spectrum antibiotic coverage, which includes vancomycin to cover *Staphylococcus* and *Streptococcus* spp., gentamicin for Gram-negative coverage, and metronidazole for anaerobic coverage. This is an effective and inexpensive regimen for vaginal surgery when the ramifications of infection are significant.

An inverted 'U' or midline incision is made in the anterior vaginal wall. The anterior vaginal wall is carefully dissected off of the pubocervical fascia, progressing laterally to the endopelvic fascia. Depending upon which bone-anchoring system is being used, the endopelvic fascia may or may not be perforated at this point: InFast® (American Medical Systems, Inc., Minneapolis, Minnesota) or Precision SpeedTac® (Boston Scientific Corp., Natick, Massachusetts). The In-Fast system implements a battery-operated bone drill that screws a titanium bone anchor behind the pubic bone (Figure 21.4A) The Precision

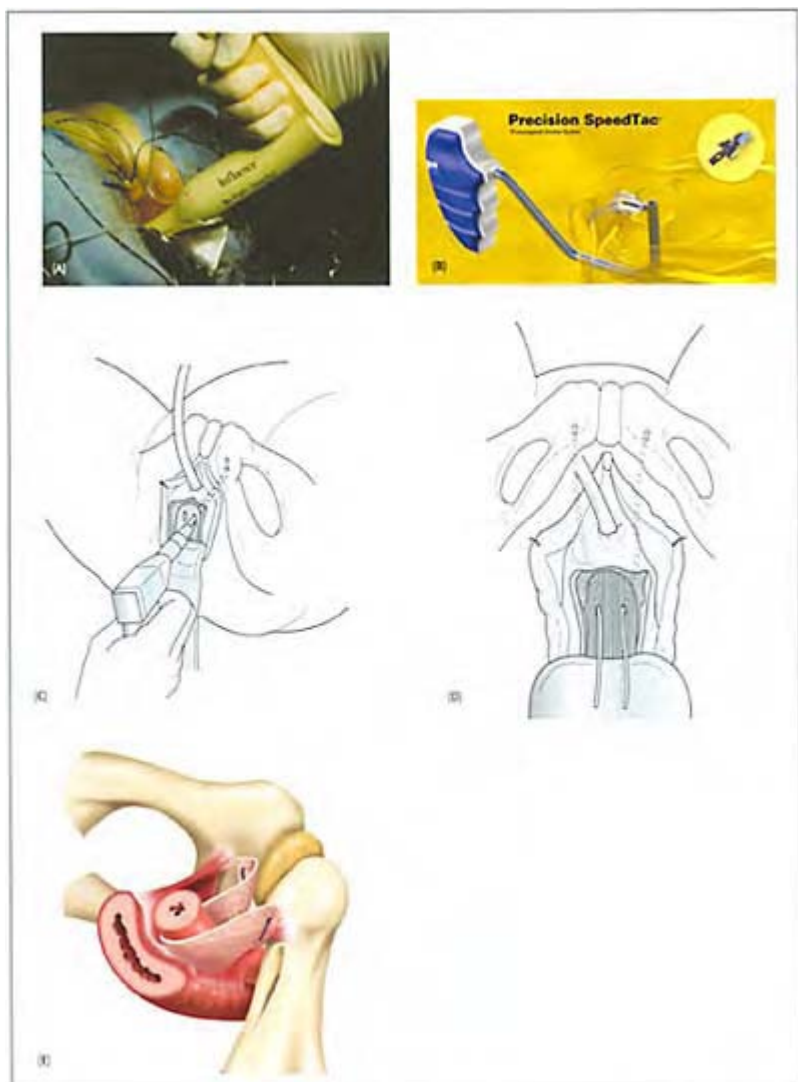
SpeedTac system utilizes a trochar-tipped anchor, which is placed securely into the pubic bone by firm backwards pressure on the delivery system, effectively functioning as a tack (Figure 21.4B). Both systems are designed with an angled delivery system, which directs the force of the anchor towards the posterior surface of the pubic bone when the surgeon pulls back on the handle.

The In-Fast system does require perforation of the endopelvic fascia for adequate positioning of the anchor behind the bone. We achieve this perforation by directing a curved Mayo scissors towards the ipsilateral shoulder just under the bone and applying gentle upwards pressure. Once the scissors enter the retropubic space, they are spread and then removed open, creating a 1–2 cm defect. The Precision SpeedTac system can be positioned with or without endopelvic fascial perforation. In cases of reoperative surgery, we prefer to perforate the fascia to ensure proper placement of the device behind the pubic bone. This is necessary because scar formation may prevent adequate anterior displacement of the intact endopelvic fascia during positioning of the device. Otherwise, we prefer not to perforate the fascia with scissors to minimize an iatrogenic paravaginal defect and preserve pelvic floor integrity. With either technique, the device should be placed, perpendicular to the bone to make direct contact with the bone prior to anchor deployment (Figure 21.4C).

The position can be confirmed by scraping the device against the bone. The anchors are typically placed 2–3 cm lateral to the urethra on either side. Anchors in either system are preattached to nonabsorbable suture material (Figure 21.4D). In the case of the In-Fast device, the anchor is preloaded with No. 1 polypropylene. The Precision SpeedTac comes with No. 1 polybutester monofilament or No. 1 braided polyester. When the insertion tools are removed, the anchor remains fixed to the bone with the double-armed suture trailing behind it. Proper anchor placement into the bone should be confirmed by pulling on the suture and finger palpation (the anchor should be nearly flush to the bone surface). Copious antibiotic irrigation of the wound is performed throughout the procedure to reduce the risk of bacterial contamination. Once the anchors are placed, the sutures are secured to the selected sling material. We favor porcine dermis over other available ‘off-the-shelf’ materials because of its superior tensile strength, easy handling, and minimal tissue reaction. A 2 cm×5 cm sling is tailored at the assistant’s table. With an 18-gauge hollow-core needle, a single limb of each suspension suture is passed through the edge of the sling material bilaterally in a ‘U’ fashion (horizontal mattress). Once placed, the sling is ready to be tied into position.

It is important at this point to remove the Foley catheter and weighted vaginal speculum. This will permit adequate urethral coaptation during sling tension adjustment. One side of the sling is then secured to the ipsilateral bone anchor by tying the suture limb that was passed through the sling to its corresponding free limb. A Kelly clamp or Mayo scissors is then positioned between the sling and the proximal urethra to act as a spacer, preventing excessive tension while allowing coaptation. The opposing sutures are then tied, bringing the contralateral end of the sling into apposition with the retropubic space. The clamp is removed and the sling is tacked at its midpoint at 6 and 12 o’clock to the perivesical and periurethral fascia, respectively, with 3–0 Vicryl. This will prevent the sling from rolling over and assure extension across the proximal urethra (Figure 21.4E). After copious antibiotic irrigation, the vaginal wall is then closed with a running/locking 2–0 Vicryl suture.

*Transvaginally bone-anchored pubovaginal slings—results:* Whenever interpreting the results of the transvaginal anchor-based slings, there are several variables to consider. First, investigators use a variety of materials and treatment failure will most often be attributed to failure of the material used for the sling rather than of the anchor. In addition, as with most clinical studies regarding stress incontinence, different authors use different criteria to assess cure. In general, in regard to bone anchors, long



**Figure 21.4** Bone-anchoring devices.  
(A) In-Fast<sup>®</sup> device (American

Medical Systems, Inc., Minneapolis). A battery-operated bone drill screws a titanium bone anchor behind the pubic bone. After perforation of the endopelvic fascia, the device is positioned into the retropubic space. Firm backwards pressure during drilling will ensure screw fixation. (B) Precision SpeedTac<sup>®</sup> (Boston Scientific Corp., Natick, Massachusetts). A trocher-tipped anchor is secured to the pubic bone by firm backwards pressure on the delivery system. Endopelvic fascial perforation is usually not necessary. (C) a transvaginal bone anchor insertion tool should be placed perpendicular to the bone and make direct contact with the bone. (D) Transvaginal bone anchors with nonabsorbable suture are attached to the undersurface of the pubic bone. The anchors are typically placed 2–3 cm lateral to the urethra on either side. (E) Bone anchored fascial sling in situ.

term follow-up is lacking. Most short- to intermediate-term studies have been encouraging. However, Elias et al reported a 92.5% rate of ‘complete cure’ in 40 patients followed for an average of 6.5 months.<sup>27</sup> Giberti et al found complete cure in 82% of patients at mean follow-up of 17 months.<sup>28</sup> Similarly, in a combined bone-anchored pubovaginal sling and cystocele repair using cadaveric fascia, Kobashi et al demonstrated an 82% cure rate after 12.4 months of followup.<sup>29</sup> In contradistinction, Carbone et al reported disappointing results using transvaginal bone anchors and cadaveric fascia, with 37.6% of patients experiencing recurrent moderate-to-severe incontinence after mean followup of 10.6 months.<sup>30</sup> This group attributed these results to failure of the material rather than of the bone anchors.

*Complications: osteitis pubis and osteomyelitis—What is the evidence?* There are several reports in the literature describing the development of osteitis pubis or osteomyelitis after use of bone anchors for sling fixation. Osteitis pubis, an inflammatory condition, will commonly occur with symptoms of suprapubic pain, pain with ambulation, malaise, and low-grade fever. Patients will often respond to treatment with anti-inflammatory drugs

and physical therapy. Osteomyelitis, an infectious condition, may have a similar presentation but will steadily progress and be unresponsive to conservative measures. Persistent drainage from the wound is nearly diagnostic. Plain radiographs of the pubis may demonstrate bony destruction. Symptoms may occur many months after surgery. The offending organism is usually *Staphylococcus epidermidis*. Nearly all cases of pubic osteomyelitis described in the literature have occurred after suprapubic bone anchor placement, with only 1 case reported after transvaginal anchoring. In a recent report of 9 cases of bone anchor-related osteomyelitis, methicillin-resistant *Staphylococcus* spp. were cultured from all patients, suggesting skin contamination of the anchor.<sup>31</sup> It is clear that prophylactic perioperative antibiotics covering *Staphylococcus* and *Streptococcus* spp. are essential. Rackley et al have reviewed the literature and found only 6 reported cases of osteomyelitis after 1018 procedures (0.6% incidence).<sup>32</sup> Given the current literature to date, the risk of pubic osteomyelitis related to transvaginal bone anchor placement is exceedingly small and maybe practically eliminated by proper perioperative antimicrobial prophylaxis.

#### **Transvaginal bladder neck suspension and pubovaginal sling to Cooper's ligament.**

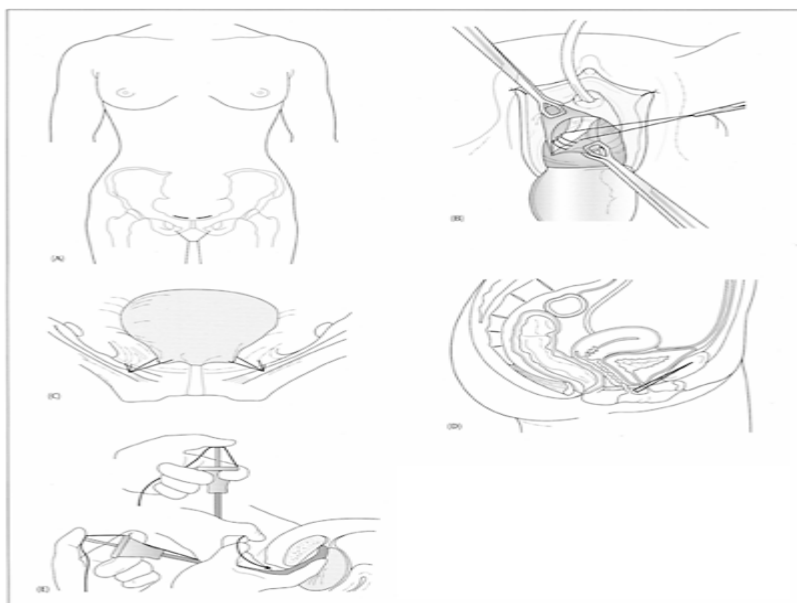
On the basis of the success of the Burch retropubic urethropexy, a completely transvaginal approach to retropubic bladder neck suspension with fixation to Cooper's ligament has been developed. This procedure as originally described had been technically challenging because of difficulties in accessing the ligament transvaginally (Figure 21.5A-D). More recently, an autosuturing device has been developed that facilitates suture placement into Cooper's ligament. This device, called the Capio® CL (Boston Scientific Corp., Natick, Massachusetts), delivers a nonabsorbable suture through Cooper's ligament using a 'push and catch' mechanism that retrieves the suture upon device removal (Figure 21.5E). Subsequently, the suture can be attached to periurethral/endopelvic fascia/vaginal wall for purposes of urothorpexy or through donor fascia or synthetic material for pubovaginal sling. Using this system, Koduri and Sand reported on 36 patients who underwent transvaginal retropubic bladder neck suspension.<sup>33</sup> Although the surgery was technically feasible, overall success with this procedure was only 70% with short-term follow-up (mean 13 months), and it was abandoned by the authors in favor of the transvaginal Cooper's ligament sling. With the sling procedure, a segment of cadaveric fascia was tied to the preplaced sutures delivered with the Capio CL device to Cooper's ligament, providing a suburethral sling. Patients who underwent a transvaginal Cooper's ligament sling using the Capio CL device and cadaveric fascia fared better than those who underwent retropubic suspension, with 83% of patients cured at short-term follow-up. Urethral hypermobility was corrected in nearly 90% of patients.

#### **Transvaginal 'tension-free' mid-urethral slings**

Midurethral synthetic slings represent a significant advance in the minimally invasive approach to sling surgery. These slings are essentially woven polypropylene mesh strips that are positioned via three small incisions (a single vaginal incision over the midurethra, and two suprapubic stab wounds, all <1.5 cm). These are 'off-the-shelf' slings with integrated delivery systems that allow rapid positioning with average operative times of less than 30 min. The main difference between the currently available systems is the method by which the slings are implanted. Many physicians have performed these

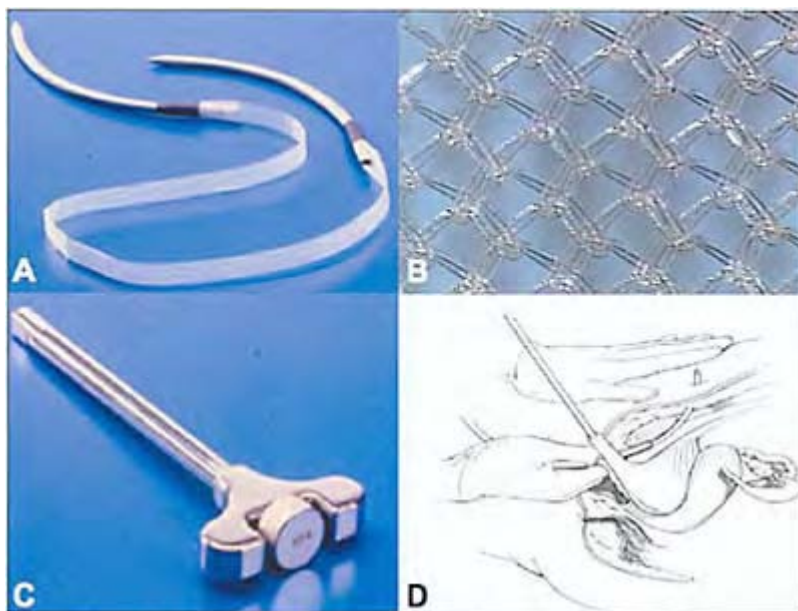
procedures safely with patients under local anesthesia. The minimal invasiveness of this technique allows most procedures to be performed on an outpatient basis.

**Tension-free vaginal tape.** The original midurethral sling introduced by Ulmsten et al in 1995, TVT® (Ethicon Inc., Somerville, New Jersey) differs from conventional pubovaginal slings in its distal positioning at the midurethra (Figure 21.6A-C).<sup>34</sup> Its proposed mechanism of action, based on Petros and Ulmsten's 'integral theory' of the pelvic floor, is reinforcement of the 'functional' pubourethral ligaments, securing the midurethra to the pubic bone and re-establishing integrated function with the suburethral vaginal hammock and pubococcygeus muscle.<sup>35</sup> More than 100,000 cases have been performed worldwide.<sup>36</sup>



**Figure 21.5** Transvaginal bladder neck suspension and pubovaginal sling to Cooper's ligament. (A) Initial bilateral suprapubic skin incisions are made to access Cooper's ligament. (B) The vaginal sling component of the pubovaginal sling to Cooper's ligament is constructed by incorporating endopelvic fascia with full-thickness vaginal tissue minus the vaginal epithelium. (C) Coronal view demonstrates sutures incorporating the

endopelvic fascia at the bladder neck.  
 (D) A sagittal view of the endopelvic fascia anchored to the Cooper's ligament. (E) Capiro<sup>®</sup> CL (Boston Scientific, Natick, Massachusetts) device, which delivers a suture through Cooper's ligament.

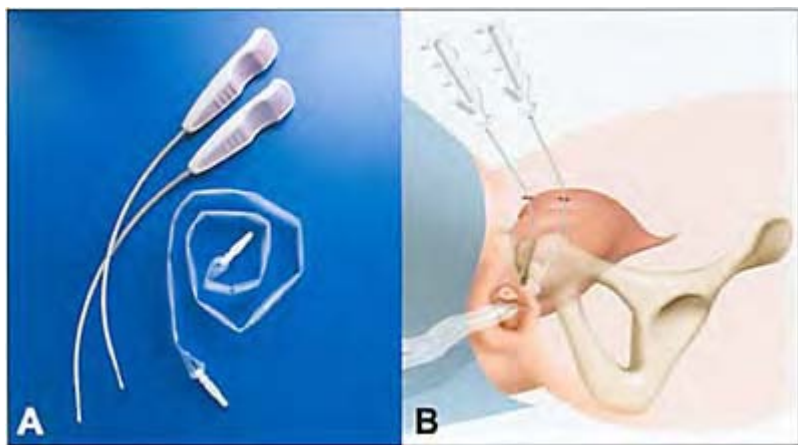


**Figure 21.6** Tension-free vaginal tape. (A) The TVT<sup>®</sup> midurethral sling system consists of two trocar needles with a preattached polypropylene mesh sling covered with removable plastic sheathing. (B) Interstices of the polypropylene mesh allows invasion of host fibroblasts and sling integration with host tissues. (C) TVT introducer attaches to trocar needles and facilitates needle passage. (D) The delivery needle is passed from the vaginal incision, through the anterior

abdominal wall incision, at all times hugging the posterior aspect of the pubic bone.

*TVT—surgical technique:* With the patient in the lithotomy position, a Foley catheter and a weighted vaginal speculum are placed after the establishment of local, regional, or general anesthesia. A 1.5 cm anterior vaginal wall incision is performed over the midurethra, followed by minimal blunt lateral dissection around the urethra to create a space for TVT needle passage. Two abdominal stab wounds using a No. 11 blade scalpel are made just above the pubic symphysis, approximately 4 cm apart on either side of the midline. Complete bladder drainage is assured. A rigid catheter guide is inserted into the Foley catheter, whose handle is deflected to the ipsilateral side of needle passage. This serves to move the bladder neck and proximal urethra away from the path of the needle. The delivery needle is then passed from the vaginal incision, through the anterior abdominal wall incision, at all times hugging the posterior aspect of the pubic bone (Figure 21.6D). With the needle in position, the Foley catheter is removed and cystourethroscopy is performed to confirm bladder and urethral integrity. Once assured, the needle is pulled through the skin, carrying the sling upwards to the anterior abdominal wall. The procedure is then repeated on the opposite side. If the procedure is performed with the patient awake under local anesthesia, some surgeons recommend a supine cough test to assist with tension adjustment.

*Suprapubic arc sling:* The SPARC® (American Medical Systems, Inc., Minneapolis, Minnesota) system (Figure 21.7) was developed to allow the transvaginal tape procedure to be performed with needle passage from above. This method is familiar to most urologists as it mimics the



**Figure 21.7** Suprapubic arc sling (SPARC®; American Medical Systems, Inc., Minneapolis, Minnesota). (A) The SPARC system



consists of specially designed needles that connect-lock to a polypropylene mesh sling preconnected to plastic fascial dilators. (B) The needles are passed from above, through suprapubic stab incisions, hugging the posterior surface of the symphysis pubis and exiting below, through the vaginal incision. The polypropylene mesh sling is then connected and pulled anteriorly into position.

traditional passage of the suspension needle used for pubovaginal slings. The theory behind this modified technique for tape placement is that it will reduce the potential risk for bowel or vascular injuries that have been reported after the TVT procedure. Clinical experience with this technique is limited to date, and no studies have been reported. Procedurally, a small midline midurethral incision is performed as for TVT. Two small suprapubic stab wounds are made with a No. 11 blade 2 cm from the midline. Specially designed SPARC needles (Figure 21.7A) are passed from above, through the suprapubic incisions, hugging the posterior surface of the symphysis pubis and exiting below, through the vaginal incision (Figure 21.7B). A single cystoscopy is then necessary to verify bladder integrity. Once confirmed, the SPARC sling is connected on either side to each needle and pulled up through the suprapubic incisions. Fascial dilators affixed to the sling system dilate the endopelvic fascia as the sling is pulled up into position. Tension is adjusted appropriately and the plastic sheath is removed, leaving the sling in place. A Prolene tensioning suture that runs longitudinally through the sling may aid in tension adjustment after the plastic sheathing has been removed.

Theoretically, results with this procedure should mimic those obtained with traditional TVT. Practical experience with this technique prompts us to make a single cautionary statement for the implanting physician. When passing needles from above during pubovaginal sling procedure, it is customary to insert a finger through the vaginal incision and into the retropubic space to guide the course of the needle. In the case of the SPARC procedure, in which the endopelvic fascia is not violated prior to needle passage, there may be a tendency to force a finger tip upwards to touch the needle, deforming the endopelvic fascia. Unfortunately this will often result in a tearing of the short midurethral incision up towards the bladder neck and affect proper midurethral sling placement and, consequently, surgical outcomes. It is our recommendation, therefore, to insert a fingertip gently into the incision, applying minimal force to meet the needle tip below the pubic bone, avoiding the potential for this complication.

*Transvaginal 'tension-free' mid-urethral slings: results:* The best candidates for these midurethral sling procedures appear to be patients with genuine SUI associated with hypermobility and leak point pressures  $>60$  cmH<sub>2</sub>O. Results for this group are reported to remain in the 80–85% range for up to 5 years.<sup>37</sup> Patients with severe ISD tend to do less well, with cure rates of approximately 74% after 4 years of follow-up.<sup>38</sup> At present, long-

term follow-up data with these procedures are generally lacking. In addition, all reports to date have been with the TVT procedure, and no studies have been published stating results with the SPARC technique. One can only assume that the SPARC will have equivalent efficacy to TVT, but this has not been proven clinically.

*Transvaginal 'tension-free' mid-urethral slings: complications:* Midurethral slings carry risks of postoperative urinary retention and voiding dysfunction similar to those of conventional pubovaginal slings. Intraoperative complications related to the TVT procedure itself are uncommon, but severe complications related to trocar placement, including major vascular injury or unrecognized enteric injury, have been reported.<sup>39-41</sup> In a large consecutive series by Kuuva et al, the most common intraoperative complication was bladder perforation, which resulted in no significant postoperative morbidity.<sup>42</sup>

### *Radiofrequency bladder neck suspension*

The efficacy of radiofrequency (RF) energy for the treatment of SUI secondary to urethral hypermobility has recently been investigated. Fulmer et al conducted a study in which thermal energy was applied laparoscopically via an RF probe to the endopelvic fascia (EPF) supporting the bladder neck and proximal urethra in patients with type II SUI.<sup>43</sup> The treatment is based on the theory that heating will result in shrinkage of the collagenous component of the EPF, resulting in the restoration of lost anatomical support. They treated a total of 94 women with type II SUI and VLPP >90 cmH<sub>2</sub>O. For the procedure, the EPF was laparoscopically cleared of surface fat, after which an RF electrothermal probe was positioned onto the periurethral endopelvic fascia and used to heat the EPF to at least 85°C. Intraoperative efficacy of the applied energy was judged by visual shrinkage of the EPF. The authors reported that 81.2% of patients were cured or improved after 12 months of follow-up. Intraoperative complications, including bladder perforation and hematoma formation, occurred in 4.3% of patients. However, these were handled laparoscopically without incident. At present, long-term follow-up in this patient cohort is lacking. Ways of delivering this treatment transvaginally and transurethrally are currently in development.

### *Laparoscopic bladder neck suspension*

Laparoscopic bladder neck suspension was originally envisioned as minimally invasive surgery that would duplicate the effective results of the open Burch colposuspension for the treatment of genuine stress incontinence. Despite early enthusiasm for the approach because of the presumed decrease in morbidity associated with the open technique, the procedure has been largely abandoned because of disappointing long-term outcomes. The first report of the procedure was by Vancaillie and Schuessler in 1991.<sup>44</sup> This intraperitoneal technique closely resembled the open Burch technique in principle. It was subsequently performed extraperitoneally by McDougall, who laparoscopically sutured the proximal urethral fascia to Cooper's ligament using No. 0 Ethibond sutures after creating a potential space using a balloon dilator.<sup>45</sup> Several other investigators have used varying approaches to perform this procedure, including the use of bone anchors and suspensory Gore-Tex mesh.<sup>46,47</sup> Universally, the procedure is considered technically challenging, with a steep learning curve, and requires a substantially longer operative

time than transvaginal needle bladder neck suspension.<sup>48</sup> Results have been generally poor, with a 30–40% cure rate after at least 36 months of follow-up.<sup>46,48</sup> Given the available alternatives, this procedure is no longer considered appropriate for the management of patients with SUI.<sup>48</sup> However, extensive reconstructive laparoscopic experience has been obtained with the development of complex laparoscopic pelvic surgery, which can potentially pave the way for the reassurance of laparoscopic bladder neck suspension.

## **Treatment of urge urinary incontinence**

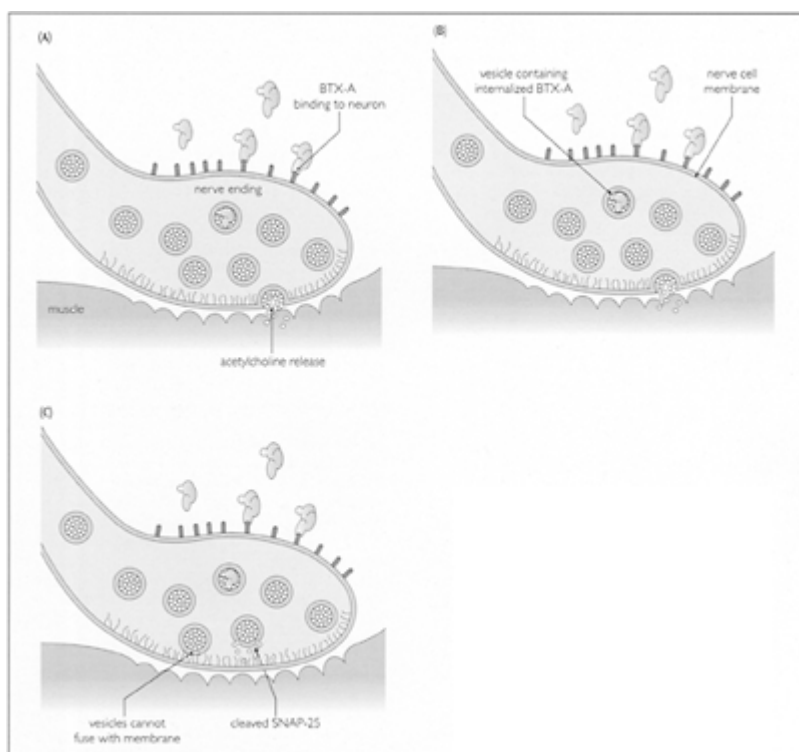
### *Nonsurgical treatment options*

Currently available pharmacologic therapies for the treatment of urgency-related incontinence due to overactive bladder are effective and should be considered the firstline treatment. Extended-release preparations of oxybutynin (Ditropan XL<sup>®</sup>) and tolterodine (Detrol LA<sup>®</sup>) are antimuscarinic agents that effectively suppress involuntary detrusor contractions while minimizing bothersome sideeffects of xerostomia and constipation. These drugs, along with adjunctive agents such as tricyclic antidepressants, should be implemented before considering surgical therapy. Behavioral therapies, including biofeedback, have also been shown to be effective in alleviating symptoms in many patients.<sup>49</sup>

### *Minimally invasive surgical therapy*

#### **Botulinum toxin A**

In recent years, several investigators have demonstrated the effectiveness of botulinum toxin A (Botox<sup>®</sup>, Allergan, Irvine, California) for the treatment of refractory detrusor hyperreflexia with incontinence.<sup>50,51</sup> Botulinum toxin A reduces or eliminates muscular contraction by inhibiting acetylcholine release at presynaptic nerve terminals of the neuromuscular junction (Figure 21.8A-C). Injection of the toxin will result in a local field denervation at the injection site.<sup>52</sup> Schurch et al reported the first clinical experience with intravesical Botox injection for the treatment of detrusor hyperreflexia.<sup>53</sup> They performed injections in 21 patients with neurogenic bladder related to spinal cord injury with severe detrusor hyperreflexia refractory to high-dose anticholinergic drugs. After a single treatment with up to 300 units of Botox, all but 2 patients were fully continent within 6 weeks after surgery. Urodynamics demonstrated significant increases in maximal bladder capacity and reflex volume as well as significant decreases in maximal detrusor pressure during uninhibited bladder contractions. A follow-up study



**Figure 21.8** Botulinum toxin A (Botox<sup>®</sup>, Allergan, Irvine, California): mechanism of action (A) *Binding*: the Botox molecule binds specifically to cholinergic nerve terminals in the neuromuscular junction. (B) *internalization*: bound toxin is internalized into the nerve terminal via a process of endocytosis. (C) *Blocking*: Internalized Botox blocks acetylcholine protein called SNAP-25, essential for transmitter release from the nerve terminal.

revealed that the effects of the toxin were durable for at least 9 months.<sup>50</sup> The procedure was safe, with no observed side-effects or adverse events reported. Franks et al later demonstrated in an animal model that botulinum toxin A injected into bladder smooth muscle resulted in decreased contractility by limiting acetylcholine and norepinephrine

release from presynaptic nerve terminals.<sup>54</sup> Chancellor et al used Botox safely in a cohort of 50 patients with voiding dysfunction, including patients with idiopathic overactive bladder symptoms and urge incontinence.<sup>51</sup> Overall, 82% of patients reported reduction or resolution of incontinence with no long-term complications. Importantly, no patient developed chronic urinary retention.

**Injection procedure.** We generally perform this procedure in an outpatient setting under local anesthesia with or without light monitored sedation. Up to 300 units may be safely injected during a treatment session. However, we generally will inject 200 units for the first treatment in most patients. Botox comes lyophilized in 100 unit vials and must be gently reconstituted in 10 ml of preservative-free normal 0.9% saline solution immediately before use. We currently use a transurethral injection system that includes a 22gauge cystoscopic needle passed through a working element with a locking system that will hold the needle securely in place. The working element is introduced into the bladder via a 22F cystoscope with 12° or 30° lens and greatly facilitates accurate injection. Ten units of toxin are injected at a total of 20 sites throughout the bladder, concentrating mostly on the bladder base and sparing the major portion of the trigone. Patients return home the same day and are followed with voiding diaries and office evaluation, including post-void residual determination.

Initial experience with Botox is extremely encouraging, with most patients reaping clinical benefit with few or no side-effects. Further studies evaluating the long-term effectiveness of this treatment method are anxiously awaited.

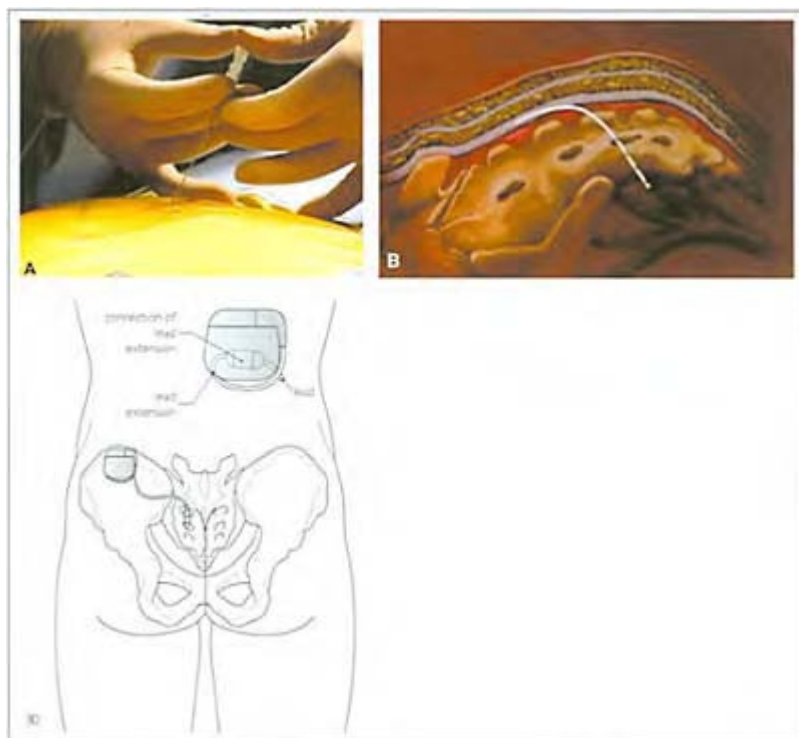
### **Sacral neuromodulation (InterStim<sup>®</sup>, Medtronic, Minneapolis, Minnesota)**

The clinical application of sacral nerve stimulation for the treatment of refractory urge incontinence by urologists can largely be credited to the work of Tanagho and Schmidt.<sup>55</sup> They based their initial human trials on accumulated knowledge from earlier animal and cadaver studies that led to a detailed understanding of the neurophysiology of the voiding reflex as well as the influence of the sacral nerves on voiding behavior.<sup>56-58</sup> Although the exact mechanism by which sacral nerve stimulation improves urinary symptoms is unknown, it is thought to induce an inhibitory reflex on the detrusor by stimulation of afferent and/or efferent pathways.<sup>59</sup> Its efficacy for the treatment of overactive bladder and urgency-related incontinence has been well documented.<sup>59,60</sup> The procedure entails permanent implantation of a quadripolar stimulating electrode into the S3 foramen next to the S3 nerve. A pulse generator, implanted and connected to the electrode, provides continuous nerve stimulation. The duration, frequency, and amplitude of stimulation can all be adjusted telepathically, as can the choice of which of the four electrodes is activated. Typically, a patient will undergo a percutaneous trial of subchronic stimulation via an external stimulator to determine the likelihood of benefit from a permanent implantation.

**Percutaneous test stimulation.** We perform all percutaneous test lead implantations in the outpatient setting with the patient under local anesthesia only. The patient is awake, in the prone position, allowing direct access to the sacrum. Although the S3 foramen may be located using bony landmarks, we have found that fluoroscopy greatly facilitates precise

placement, shortening the procedure and limiting patient discomfort. Use of a C-arm is optimal, as this will allow both A-P (anteroposterior) and lateral views of the sacrum. Under fluoroscopy, the S3 foramen is consistently present at the inferior margin of the sacroiliac joints, 1 cm from the midline. Local anesthesia is established at a point approximately 1 cm cephalad to the foramen as the 21-gauge spinal needle used for lead introduction must enter the superior margin of the foramen at a 60° angle to the skin (Figure 21.9A). Once the needle enters the foramen, external stimulation is performed and the needle depth is adjusted to provide optimal sensory and motor responses. With a well-positioned needle, the patient will report sensation of stimulation in the perineum, rectum, and/or vagina only. Motor response, indicating correct placement in the S3 foramen, includes a bellows-like inward pulling of the levator ani muscle and flexion of the ipsilateral great toe. Once adequate needle positioning is obtained, a temporary lead is passed through the needle under fluoroscopic guidance and the needle is removed. The electrode is stimulated to test for adequate placement, taped securely into position, and connected to an external stimulator which may be worn on the patient's belt buckle. The patient is sent home with the stimulator on continuously for a period of 3–7 days, during which time a detailed daily voiding diary is completed. When the patient returns for lead removal, the voiding diary is compared with a pretest diary. Motivated patients who experienced at least a 50% reduction in urge incontinent episodes are offered permanent implantation.

**Permanent lead implantation.** Recent modifications in the technique of permanent lead placement (Figure 21.9B) have made the procedure exceedingly minimally invasive. Previously, electrode placement required suture fixation to the sacral periosteum to assure lead stabilization, reducing



**Figure 21.9** Sacral neuromodulation therapy (InterStim<sup>®</sup>, Medtronic, Minneapolis, Minnesota). (A) Percutaneous test stimulation: A 21-gauge spinal needle implemented for lead introduction must enter the superior margin of the foramen at a 60° angle to the skin. Once the needle enters the foramen, external stimulation is performed and the needle depth is adjusted to provide optimal sensory and motor responses. (B) A permanent quadripolar lead is inserted into the S3 foramen and optimally lies parallel to the nerve. (C) Quadripolar lead and pulse generator in situ post-implantation.

the risk of migration out of the S3 foramina. For this, a sizable midline sacral incision with division of the lumbodorsal fascia and underlying paravertebral muscles was required, which necessitates general anesthesia and results in moderate postoperative discomfort. Presently, a specially designed self-anchoring tined lead has been developed that can be placed percutaneously under local anesthesia only. This has resulted in shorter surgical time and faster patient recovery and has made lead placement less technically demanding. For tined lead placement, the patient is placed in the prone position, as for the percutaneous test stimulation. Local anesthesia is established. The spinal needle is placed into the desired S3 foramen under fluoroscopic guidance and tested. Sensory and motor responses are elicited to ensure appropriate placement. A wire directional guide is then passed through the needle into the foramen using the Seldinger technique. The needle is removed and the tip of a No. 11 blade is used to make a stab wound approximately 5 mm in size. A fascial dilator with introducer sheath is then advanced over the directional guide into the S3 foramen. The directional guide and dilator are removed, leaving the introducer sheath in place. The tined lead is then positioned within the foramen under fluoroscopic guidance and test stimulated to assure adequate nerve contact. Finally, the introducer sheath is removed, resulting in tine deployment and lead stabilization. Once the lead is in position, the InterStim pulse generator is placed subcutaneously into the upper buttock. This is usually accomplished with a 3.5 cm skin incision. A tunneling tool is used to transfer the lead from the midline to the buttock incision, where final connections are completed (Figure 21.9C).

**Two-staged permanent implant.** A two-staged permanent implant procedure has been developed to attempt to reduce the likelihood of an inconclusive or falsely negative percutaneous test stimulation due to lead migration. The first stage involves permanent lead implantation into the S3 foramen, as previously described. The lead is tunneled to the region of the prospective neurostimulator site. An extension lead is connected at this site and is then tunneled to the opposite side, where it exits the skin. The extension lead is then connected to an external test stimulator identical to the one used in percutaneous testing. Placement of the permanent lead virtually eliminates artifactually negative results. The extension lead is used to reduce the risk of infection. After a 3–5 day trial period, if the patient experiences significant benefit, the second stage is performed. This involves placement of the pulse generator in the upper buttock with lead connection as previously described. The lead extension is removed. When this technique was used, the testing phase resulted in an 80% success rate.<sup>61</sup>

**Results:** A number of investigators have reported success with sacral nerve stimulation for the treatment of refractory urge incontinence due to detrusor hyperreflexia.<sup>59,60,62</sup> Most studies report successful percutaneous test stimulation in approximately 50% of patients. Janknegt et al demonstrated that up to 80% of patients who failed the percutaneous test stimulation may have a favorable response to the staged approach to implantation.<sup>61</sup> Schmidt et al conducted a multicenter prospective randomized study that found 47% of patients completely dry at 6 months after implantation.<sup>59</sup> An additional 29% of patients experienced a greater than 50% reduction in incontinence episodes. The percent of patients either dry or improved was thus 47%+29% or 76%. This is especially dramatic, considering that these were patients with severe urge incontinence, previously unresponsive to all prior medical therapy. During this trial, all patients who responded to InterStim therapy underwent a therapy evaluation test in which the device was inactivated



for a minimum of 3 days. In all patients, symptoms returned to their preimplantation baseline, confirming the efficacy of active stimulation. Janknegt et al reported sustained longterm clinical efficacy in this cohort of patients, with the majority of patients who experienced successful outcomes at 6 months having persistent benefit at mean follow-up of nearly 3 years.<sup>60</sup> Side-effects or adverse events were minimal and included pain at the generator or lead site, lead migration, and infection. Bosch and Groen reported their results on a similar cohort of patients with refractory motor urge incontinence.<sup>62</sup> They performed permanent implantation on 45 patients who had a favorable response to percutaneous stimulation. At mean follow-up of 47 months, 60% of patients were either dry or improved. Interestingly, follow-up urodynamics revealed that approximately half of the patients who had persistent instability were still clinically cured, suggesting that the abolition of instability is not an absolute requirement for symptomatic relief.

### **Laparoscopic enterocystoplasty**

Bladder augmentation or enterocystoplasty is most commonly employed for the treatment of the small-capacity, poorly compliant, hyperreflexic neurogenic bladder. For the non-neurogenic patient with refractory urge incontinence it is often considered a procedure of last resort and should be reserved for patients who have failed less-invasive surgical therapy. When utilized, however, the procedure is exceedingly effective in increasing bladder capacity and eliminating urgency and urge incontinence. As interposition of bowel into the urinary tract may significantly reduce overall bladder contractility, patients should be advised of the potential risk of chronic urinary retention postoperatively necessitating lifelong intermittent catheterization.

Experience to date with laparoscopic enterocystoplasty is limited, with the first complete procedure being performed within the last 8 years. It is clear from the existing urologic literature on the subject that the procedure is technically challenging and requires advanced laparoscopic skills. Docimo et al performed the first completely laparoscopic enterocystoplasty on a 17-year-old girl with neurogenic bladder and sacral agenesis using a segment of stomach.<sup>63</sup> Stomach was chosen by this group for the augmentation as it would be easily harvested and avoid the necessity of bowel anastomosis. The procedure was accomplished, along with laparoscopic bladder neck suspension, using a total of four 12 mm cannulas and a single 5 mm cannula over a period of nearly 11 hours. Automated stapling and suturing devices aided in the harvesting and anastomosis of the 20 cm stomach patch used in the augmentation. The patient had an initial successful outcome with a doubling of her bladder capacity and significant reduction in compliance, allowing her to catheterize every 4 hours and remain dry.

However, this same group, when later reporting their accumulated experience with laparoscopic-assisted reconstructive urologic surgery, seemed to have abandoned the use of stomach for laparoscopic gastrocystoplasty and, in fact, performed a takedown of the previously reported gastric augment in favor of an ileal enterocystoplasty because of refractory hematuria-dysuria syndrome.<sup>64</sup> They performed ileocystoplasty via a Pfannenstiel or lower midline incision and used laparoscopy specifically for patients who required appendiceal harvesting for use as a catheterizable stoma. The authors advocated

reserving laparoscopy for bowel mobilization with or without appendiceal harvesting in patients requiring enterocystoplasty.

Our own practical experience with open enterocystoplasty using ileum or sigmoid colon has demonstrated, however, that these procedures can be performed without difficulty through a Pfannenstiel incision with minimal need for bowel mobilization, thus bringing into question the benefit of laparoscopy in these instances. Gill et al reported successful laparoscopic enterocystoplasty in 3 patients with neurogenic bladder using a four-port transperitoneal approach<sup>65</sup> (Figure 21.10A-D). Ileal, sigmoidal, and cecal segments were all employed for augmentation as well as creation of a catheterizable continent ileal stoma in 1 patient. The bowel segments were mobilized laparoscopically. Bowel preparation, reconfiguration, and enteric anastomosis, however, were performed extracorporeally through a 2 cm extension of the 1.2 cm umbilical port incision. The bowel was then returned to the abdominal cavity and anastomosed to the bladder laparoscopically. Total time for the procedures averaged nearly 7 hours, with the laparoscopic enterovesical anastomosis taking an average of 2 hours. Average hospital stay for the 3 patients was 5 days.

More recently, Meng et al and Elliott et al described their technique of complete laparoscopic ileal cystoplasty<sup>66,67</sup> (Figure 21.11A-D). No authors have yet published accumulated operative results with this procedure; however, using their technique, they perform bowel mobilization, isolation, and side-to-side ileal anastomosis completely intracorporeally using a total of five ports. The mesentery is divided using laparoscopic coagulating shears. Bowel isolation and anastomosis is then accomplished with an endoscopic gastrointestinal anastomotic stapler. The ileal segment is prepared, detubularized, reconfigured into a Ushape, and anastomosed to the open bladder using laparoscopic suturing techniques. A single case report by the authors indicated that the procedure took approximately 9 hours. No information was provided in terms of postoperative recovery, length of hospital stay, or cost of the procedure. Given the aforementioned accumulated experience with laparoscopic enterocystoplasty to date, it is unclear whether it provides any clear benefit over the conventional open technique. Further refinements in the technique and continued surgical experience may lead to shorter surgical times and decreased patient morbidity and in the future potentially provide an advantage over open surgery.

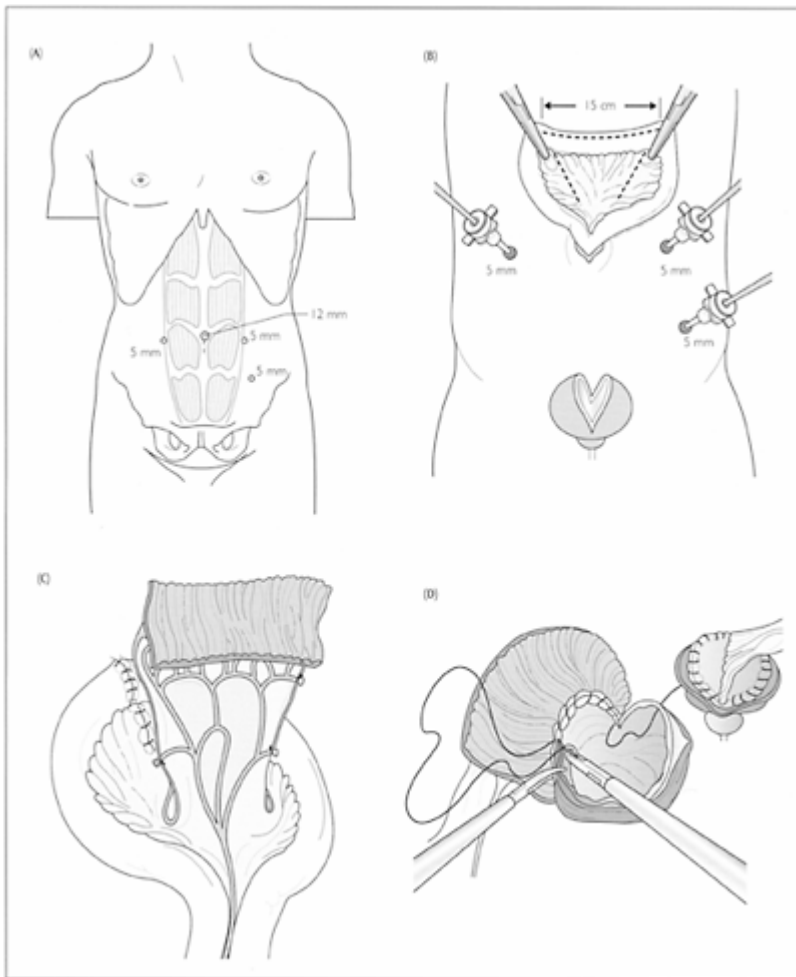
## **MINIMALLY INVASIVE APPROACHES TO PELVIC FLOOR DYSFUNCTION**

Pelvic floor dysfunction (PFD) is a general term describing conditions which may result in abnormalities of female voiding and defecatory function, as well as pelvic prolapse and chronic pelvic pain. For the purposes of this discussion we will focus primarily on minimally invasive treatments directed at the resolution of voiding dysfunction, specifically chronic urinary retention related to pelvic floor spasm.

### **Urinary retention related to external sphincteric spasticity: the non-relaxing sphincter**

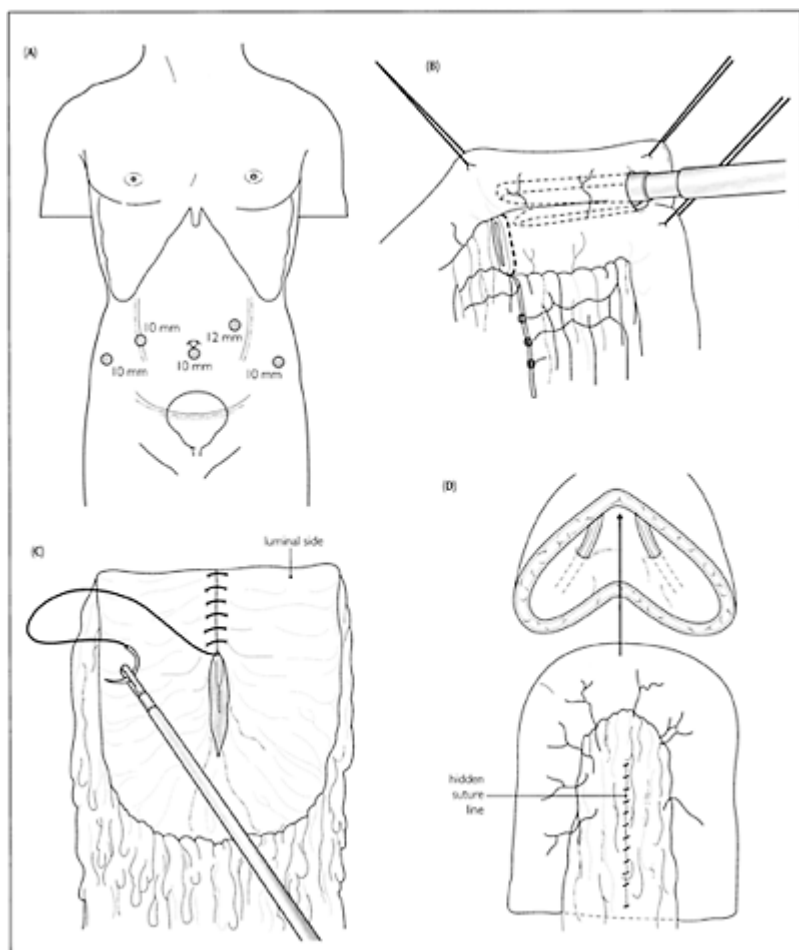
Young female patients occasionally come to the urologist with symptoms of chronic urinary urgency and frequency, and symptoms associated with obstruction, including

hesitancy, intermittency, weak stream, and sensation of incomplete emptying. Office evaluation may reveal an elevated post-void residual urine and, often, significant levator tenderness to palpation. These patients require a thorough videourodynamic investigation, including pelvic floor EMG to determine the presence of occult pelvic floor spasticity. This phenomenon, first described by Fowler et al, will manifest on videourodynamics as 'pseudodyssynergia' with markedly elevated EMG activity of the external urethral sphincter after the onset of a detrusor contraction.<sup>68</sup> Fluoroscopy will reveal bladder outlet obstruction at the level of the external urethral sphincter reminiscent of detrusor-external sphincter dyssynergia (DESD). Voiding pressures are elevated and the detrusor muscle itself may be unstable with frequent uninhibited contractions.<sup>69</sup> It is important in these patients to perform a complete neurologic examination as well as screening magnetic resonance imaging (MRI) of the spine to rule out occult neurologic diseases such as multiple sclerosis. Once neurologic causes have been excluded, the diagnosis of idiopathic chronic urinary retention or 'pseudodyssynergia' may be established. The etiology of this disorder is unknown but it may arise in some as a pathologic unconsciously 'learned' chronic activation of the guarding reflex after a bout of severe cystitis in which dysuria resulted in conscious withholding during the process of voiding and



**Figure 21.10** Laparoscopic-assisted enterocystoplasty. (A) Trocar placements for laparoscopic-assisted enterocystoplasty. (B) Ileum is brought out through the enlarged umbilical port site to harvest the flap for the bivalved bladder. (C) This illustration demonstrates augmented ileal flap with reanastomosed ileum. (D) Ileovesical anastomosis performed by a

continuous running full-thickness  
laparoscopic free-hand suturing.



**Figure 21.11** Pure laparoscopic ileal cystoplasty. (A) Trocar placement for pure laparoscopic ileal cystoplasty. (B) Ileal reanastomosis with endoscopic gastrointestinal anastomotic stapler after harvesting an ileal flap for pure laparoscopically ileal cystoplasty. (C) Intracorporeal construction of ileal flap by approximating the nonmesenteric

edge of the open ileum. (D)  
 Approximation of ileal flap to the  
 bivalved bladder with a running suture.

became imbedded in the neural circuitry. In severe cases, complete urinary retention may result, perhaps because of overinhibition of the voiding reflex by a pathologic reflex from the pelvic floor.<sup>70</sup> Until recently, this disorder could only be managed with chronic intermittent catheterization.<sup>71</sup> Conservative treatments such as skeletal muscle relaxants, biofeedback, and alpha-blockers are reasonable first efforts but are often ineffective.

### **Sacral neuromodulation**

InterStim therapy has been used successfully by several investigators for the treatment of chronic, nonobstructive urinary retention.<sup>72–75</sup> By what mechanism this therapy is able to function simultaneously for the treatment of urgency incontinence and urinary retention is unknown. It is believed that the stimulation results in a modulation of the sensory limb of the voiding reflex, allowing sphincteric relaxation and triggering of detrusor contractility by breaking the inhibitory stimulus of the abnormal guarding reflex.<sup>75</sup> Shaker and Hassouna reported restoration of voiding function in 20 patients with chronic nonobstructive urinary retention treated with sacral neuromodulation.<sup>70</sup> All patients experienced more than 50% improvement in voided volumes and post-void residual volume as well as subjective improvement in all voiding symptoms. All patients voided normally on 6-month postoperative pressure flow studies. Interestingly, patients who had concurrent complaints of chronic pelvic pain experienced a more than 50% reduction in their symptoms by weighted score comparison as well.

Jonas et al performed the first multicenter, prospective randomized study evaluating the efficacy of sacral nerve stimulation for urinary retention.<sup>75</sup> A total of 177 patients with urinary retention were enrolled. As with the urgency incontinence indication, a 3–7 day percutaneous test to assess potential response to therapy was performed in all patients. A total of 68 patients, or 38% of the original cohort, qualified for implantation by experiencing a greater than 50% improvement in baseline voiding symptoms that was lost upon removal of the temporary electrode. Thirty-seven patients were randomly assigned to receive a permanent implant, while 31 patients remained on standard medical therapy for 6 months followed by delayed implantation if clinically indicated. The treatment group demonstrated significant reduction in post-void residual volumes and a significant improvement in voided volumes relative to the control group. The effect of the therapy was lost when the device was inactivated, demonstrating the necessity of continued stimulation for efficacy. The response to therapy was durable to the longest point of follow-up (18 months). Impressively, 58% of patients with implants were able to stop intermittent catheterization completely and 71% had a reduction in post-void residual volumes by at least 50%. Complications were few and were related to pain at the stimulator or lead site or infection. From these data it is clear that sacral neuromodulation is effective and represents a significant advance in our ability to treat patients with idiopathic urinary retention potentially related to pelvic floor spasticity. The procedure is minimally invasive, safe, and completely reversible.

### Botulinum toxin A

Despite earlier disappointing results reported by Fowler et al regarding the use of botulinum A toxin for the treatment of urinary retention in females related to non-neurogenic external sphincter spasticity, the toxin has been used effectively for this purpose.<sup>76</sup>

On the basis of multiple successful reports using Botox for the treatment of DESD in spinal cord injured male patients, Phelan et al performed transurethral botulinum A toxin injections into the external sphincter of 4 women and 4 men with chronic voiding dysfunction related to non-neurogenic sphincteric spasticity.<sup>77–80</sup> In the same study, an additional 13 patients with DESD were injected during the same time period. All patients were catheterdependent preoperatively. A total of 80–100 units of botulinum A was cystoscopically injected deeply into the external sphincter at the 3, 6, 9 and 12 o'clock positions in equally aliquoted volumes. Average surgical time per procedure was 8 min. In all but 1 patient, the treatment resulted in a resumption of spontaneous voiding. Nineteen of the 21 patients treated were able to discontinue catheterization postoperatively. Two-thirds of the patients noted significant subjective improvement in voiding ability. Postoperative residual volumes decreased by 71%. The duration of therapeutic effect from an injection can be variable and in this series of patients lasted anywhere from 3 to 16 months at last follow-up. This study clearly revealed that non-neurogenic urinary retention related to external sphincteric spasticity can be effectively treated with Botox.

### Conclusions

From the preceding discussion it is readily apparent that minimally invasive therapeutic approaches directed at female urinary incontinence and pelvic floor dysfunction are possible and effective. While maintaining surgical efficacy, they have succeeded in limiting patient morbidity, speeding recovery, and hastening return to the workplace. In the decade to come, these procedures may replace their predecessors as the standards of care.

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## Interstitial cystitis

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Our understanding of interstitial cystitis (IC) has advanced dramatically in the past several years. Recent studies have yielded a volume of data that have made it possible to develop a new and evidence-based view of the causes of IC, the true prevalence of the disease, and the keys to its effective management. Although IC was once considered a disorder that was both rare and difficult to treat, we now know that it is a surprisingly common problem that can be recognized and treated with a high degree of success. This chapter reviews recent developments in the diagnosis and treatment of IC: chief among these are a newly validated symptom questionnaire and an extremely promising intravesical treatment that provides immediate and sustained relief of IC pain and urgency.

### Definition and prevalence

IC is a clinical syndrome of urinary urgency/frequency and/or pelvic pain in the absence of an identifiable cause such as bacterial infection or a history of radiation to the bladder. In the past, it was believed that IC affected the bladder only, and was a relatively uncommon problem. Recent data have transformed both our definition of IC and our understanding of its prevalence.

The traditional diagnostic criteria for IC,<sup>1</sup> which were developed for research purposes, describe the intense and unremitting pain and urinary urgency of advanced disease. IC tends to develop gradually, however, as we will describe in the Presentation section. Advanced cases represent only perhaps 2% of the individuals who have the disease. In the majority (98%) of affected patients, IC probably goes unrecognized when the traditional diagnostic criteria are used. In addition, new data indicate that IC may affect lower urinary tract tissues other than the bladder. The disease appears to arise from a pathophysiologic process that can also occur in the urethra and prostate, creating analogous conditions in those tissues (see Pathogenesis section); i.e. the disease we have called IC may affect large numbers of patients whose bladder-origin symptoms have been mistaken for signs of other disorders (see Presentation section).

Thus, there may be many cases of IC that are not reflected in the estimates from traditional urologic prevalence studies. The most recent such study, published by Curhan and coworkers in 1999, indicated that approximately 750,000 individuals in the United States have IC.<sup>2</sup> For example, new data indicate that IC may be present in as many as 81% of gynecologic patients who have chronic pelvic pain.<sup>3,4</sup> Chronic pelvic pain affects

14.7% of US women aged 18–50 years, or 9.2 million women, according to 1993 census numbers.<sup>5</sup> If we extrapolate from our findings in gynecologic patients, then 81% of these women, or nearly 7.5 million, have IC. This total itself is probably a minimum number, because it reflects 10-year-old census data and includes neither patients who have urgency only nor young women who are between menarche and the age of 18. In 2002, we published the results of a study in which we screened a general population sample with a new IC symptom questionnaire, the Pelvic Pain and Urgency/Frequency Patient Symptom (PUF) Scale, and found data indicating that IC may occur in approximately 1 of 4.5 women.<sup>6</sup> We believe these numbers are more reflective of the true prevalence of the disease.

### Presentation

In our clinical experience with over 5000 IC patients, we have found that the disease is best regarded as a continuum. Typically, it is a gradually progressive disorder whose symptoms tend to be intermittent and relatively mild in the early stages. The symptoms generally become both more intense and more constant with time.<sup>7–10</sup> In early IC, urinary urgency tends to be the principal symptom. Of recent IC patients in our clinic, at least 30% had urgency and no pain. IC patients who do have urgency may not report it because their frequency of urination is normal for them.

As time goes on, pain of increasing severity becomes the more dominant symptom in IC. For most IC patients who decide to see a doctor, the driving force is pain rather than urgency. The pain of IC may be felt in any one or more locations in the pelvis in any combination, including the urethra, the vagina (in women), the penis, testes, and/or scrotum (in men), the suprapubic area, the lower abdomen, the lower back, and the inguinal area.<sup>7,8</sup> It has been shown that the bladders of individuals with more advanced IC contain more pain fibers than those of individuals who have early or mild disease.<sup>11</sup> In the early phases of IC, pain is usually intermittent. It presents as a sudden flare that may last for days to weeks and then remit.

The character of IC symptoms varies not only from patient to patient but also from one day to the next in a single individual. Symptom severity depends not only on the stage of the disease but also on the activity of factors that provoke symptom flares, including hormonal fluctuations and seasonal allergies.<sup>7,9,12,13</sup> As we will describe, variable pathophysiologic factors determine whether an individual has pain or urgency or both, as well as where the patient feels the pain.

For all of these reasons, IC symptoms are often attributed to another urologic or gynecologic problem. Early IC may be mistaken for recurrent bladder infections or chronic pelvic pain, particularly dyspareunia. Dyspareunia, in fact, is almost always due to IC. An IC patient may receive a diagnosis of 'urethral syndrome,' which actually is early IC;<sup>7</sup> or 'urethritis' or 'nonspecific urethritis.' Recent studies indicate there may be previously unsuspected numbers of IC patients among several other clinical populations. These include women who consult gynecologists for chronic pelvic pain,<sup>3,4</sup> as mentioned above, as well as men with prostatitis<sup>14</sup> and older men who have lower urinary tract symptoms (LUTS) and are being evaluated for possible bladder outlet obstruction (BOO).<sup>15</sup> As we will describe, what underlies the symptoms in all these populations is a

single pathophysiologic process, currently fragmented into multiple diagnoses. By traditional diagnostic criteria, only the patients with the most severe symptoms were given the diagnosis of IC. In fact, however, IC is probably present in the majority of patients who are under age 50 and have urinary urgency and/or pelvic pain in the absence of any other identifiable cause.

### Pathophysiology

Several different pathologic mechanisms have been proposed for the symptom complex that is known as IC. According to an increasing body of data, bladder epithelial permeability and urinary potassium appear to play a key role in the development of many cases of the disease.<sup>16</sup> In the healthy bladder, a mucus layer containing glycosamino glycans (GAGs) forms a barrier that prevents urine and its contents from leaking through the urothelium and damaging the underlying nerves and muscle.<sup>17</sup> In most individuals with IC, however, the urothelium is abnormally permeable due to an epithelial dysfunction. The 'leaky' epithelium allows potentially harmful substances in urine to penetrate the bladder muscle, depolarizing sensory nerves and causing the symptoms as well as the progression of IC. Potassium, which occurs in high concentrations in normal urine, does not damage or penetrate a healthy urothelium but is highly toxic to tissues such as the bladder muscularis. On the basis of this epithelial permeability model, we developed the potassium sensitivity test (PST; see Diagnosis section) to enable the clinician to test for abnormal bladder epithelial permeability.

This same cycle of altered epithelial permeability, potassium leak, and nerve depolarization, if active in urethral and prostatic tissues, could give rise to symptoms that may be mistaken for signs of urethritis or prostatitis. To investigate this possibility, we tested for abnormal epithelial permeability in 44 men who had been diagnosed with and previously treated for National Institutes of Health prostatitis-chronic pelvic pain syndrome (CPPS) category III A or IIIB.<sup>14</sup> In 37 of the 44 men (84%), we found abnormal urothelial permeability, as indicated by a positive PST, a rate similar to that seen in IC patients (79%). These findings support our hypothesis that prostatitis and IC are a continuum of lower urinary epithelial dysfunction. Like individuals who have IC, most of the prostatitis patients in our study reported experiencing pain with sex, as well as pain in a variety of locations throughout the pelvis.

Another important component in the pathogenesis of IC is neurologic up-regulation. The progression of IC appears to be accompanied by significant activation of sensory nerves in the bladder.<sup>18-20</sup> This neural activation produces symptoms whose pattern in each patient is determined by whether the activation takes place in sensory nerves for pain, for urgency, or for both. Neural upregulation may result from peripheral nerve stimulation and/or injury from potassium, nerve regeneration and growth of new nerve fibers, and/or central activation of the sacral reflex arc. Interactions with mast cells may also promote this cascade.

Mast cells are believed to play an important role in IC as well,<sup>21</sup> although the precise mechanism for their involvement has not been defined. The role of mast cells may be causative or secondary or both. As causative factors, mast cells could produce the symptoms of IC by degranulating. It is also possible, however, that the mast cells are a

response to the factor(s) causing the IC: e.g. an epithelial leak. If the latter is true, the mast cell response ultimately may become part of the problem in that mast cell degranulation itself might cause an epithelial leak.<sup>22</sup>

Factors in urine may also play a role in the pathogenesis of IC, either by injuring the urothelium or by promoting its protective and reparative functions. Keay and coworkers<sup>23</sup> have reported an antiproliferative factor (APF) that may represent an alteration of the protective factors involved in normal urothelial maintenance, reducing the ability of the urothelium to proliferate and repair itself. Hurst et al have reported diminished GAG levels in patients with IC. This may be another instance of a reduction in a protective material: in this case, the GAG.<sup>24</sup> With regard to diagnostic techniques for IC, some mediators may be present in individuals who have IC that are not normally present, such as mast cell mediators and increased kallikrein. Mast cell mediators may represent abnormal mast cell activity, which, in and of itself, is inducing an altered epithelial permeability that leads to disease, as we have mentioned. The kallikrein increase may reflect increased inflammatory activity.<sup>25</sup> It has also been reported that substance P is increased in IC patients vs normal control patients and reflects the increased sensory nerve activity seen in the disease.<sup>26</sup>

It has also been reported that urine contains toxic cations that may injure urothelium, and that Tamm-Horsfall protein (THP) may function as a protective factor capable of electrostatically binding such potentially harmful cations. It has been shown that these toxic factors can be neutralized by heparin and pentosan polysulfate (PPS) and are of low molecular weight. In addition, the THP of normal control subjects was found to be more effective as a protective agent than the THP of IC patients relative to these cations and a similar toxic cation, protamine sulfate, in cultured urothelial cells.<sup>27</sup>

Another factor that may figure in the pathophysiology of this disease is vascular insufficiency. Reduction of vascular perfusion may negatively affect mucosal, muscle, and nerve nutrition and initiate a cascade of events that causes symptoms. It is known that radiation impairs blood supply by injuring the microvasculature of organs. Certainly, in the case of the urinary bladder, radiation leads to a syndrome of urgency, frequency, and altered epithelial permeability that is basically IC.<sup>28</sup> Other profusion abnormalities such as reflex sympathetic dystrophy<sup>29</sup> may result in a secondary decrease in blood flow that also triggers events leading to symptoms of the IC syndrome. Vascular injury may be accelerated in IC as a result of abnormal epithelial permeability, allowing urinary potassium to leak into the bladder interstitial space. The potassium would be directly toxic to the small blood supply of the subepithelial tissues, leading to further bladder destruction.

## Prostatitis

An accumulating body of data suggests that prostatitis is a part of the IC complex. As mentioned above, abnormal bladder epithelial permeability has been demonstrated in males who have prostatitis, and this process is probably also ongoing in the prostatic ducts. Compared to women who have IC, men with prostatitis have approximately the same mean age at diagnosis (39–48 years old) and the same (or analogous) pain locations: the perineal, abdominal, testicular, and penile areas (Table 22.1). These men

also have an abnormal American Urological Association (AUA) Symptom Score, suffer from dysuria, and have a rate of symptom flares associated with sex that is comparable to that of female IC patients. On cystoscopy, 67% of men with prostatitis have no inflammation and 60% have glomerulations. Seventy-five percent have symptom remissions after hydrodistention.<sup>30–32</sup>

The Chronic Prostatitis Study Group (CPSG) has evaluated the efficacy of PPS, a known treatment for IC, in treating males with CPPS or prostatitis. A 40% improvement was seen after approximately 4–6 months of PPS therapy,<sup>33</sup> an outcome identical to the results seen in IC patients. The CPSG has also reported the results of a double-blind study in which a 40% improvement was obtained with PPS vs 18% improvement with placebo in 74 subjects studied.<sup>34</sup> Again, these results are identical to the published results for PPS in IC. In essence, it appears that the only difference between a male diagnosed with prostatitis and a female diagnosed with IC is in gender. In symptomatology, clinical findings, and treatment outcomes, the two groups are identical.

## Diagnosis

IC is probably one of the easiest disorders for the clinician to diagnose. Contrary to the widely prevalent notion that the diagnosis of IC is one of exclusion, we have found that IC pathophysiology is indeed present in most people who have IC symptoms and are aged 55 years or younger. The

**Table 22.1** *Pain locations reported by patients with prostatitis.*<sup>a</sup>

| Location      | Patients affected (%) |
|---------------|-----------------------|
| Dysuria       | 78                    |
| Perineal      | 27                    |
| Lower abdomen | 42                    |
| Testicular    | 50                    |
| Scrotal       | 36                    |
| Rectal        | 33                    |
| Post void     | 50                    |

<sup>a</sup>Data from Parsons and Albo.<sup>14</sup>

diagnosis is based on the presence of the characteristic pattern of symptoms of urgency, frequency, and/or pelvic pain in any combination. A patient may have only urgency or only pain, but most patients have elements of both. These may be persistent or intermittent, in any combination. Similar symptomatology could come from only a small number of other disorders that should be ruled out: these are urinary tract infection (urinalysis or culture), BOO in older males, and rare instances of carcinoma of the bladder in the presence of hematuria. In addition to regular urinalysis, cytology, and cystoscopy where appropriate, two new tools can be helpful to the clinician. These are a new validated symptom scale, the PUF Scale (Figure 22.1), and the well-documented PST (Figures 22.2–22.3).



| PELVIC PAIN AND URGENCY/FREQUENCY PATIENT SYMPTOM SCALE  |       |              |          |        |     |               |              |
|--|-------|--------------|----------|--------|-----|---------------|--------------|
| Please circle the answer that best describes how you feel for each question  |       |              |          |        |     |               |              |
|  | 0     | 1            | 2        | 3      | 4   | SYMPTOM SCORE | BOTHER SCORE |
| 1. How many times do you go to the bathroom during the day?  | 3-6   | 7-10         | 11-14    | 15-19  | 20+ |               |              |
| 2. a. How many times do you go to the bathroom at night?   | 0     | 1            | 2        | 3      | 4+  |               |              |
| b. If you get up at night to go to the bathroom, does it bother you?   | Never | Occasionally | Usually  | Always |     |               |              |
| 3. Are you currently sexually active.<br>YES _____ NO _____  |       |              |          |        |     |               |              |
| 4. a. IF YOU ARE SEXUALLY ACTIVE, do you now or have you ever had pain or symptoms during or after sexual intercourse?   | Never | Occasionally | Usually  | Always |     |               |              |
| b. If you have pain, does it make you avoid sexual intercourse?  | Never | Occasionally | Usually  | Always |     |               |              |
| 5. Do you have pain associated with your bladder or in your pelvis (vagina, labia, lower abdomen, urethra, perineum, testes or scrotum)?   | Never | Occasionally | Usually  | Always |     |               |              |
| 6. Do you still have urgency after you go to the bathroom?   | Never | Occasionally | Usually  | Always |     |               |              |
| 7. a. If you have pain, is it usually  |       | Mild         | Moderate | Severe |     |               |              |
| b. Does your pain bother you?  | Never | Occasionally | Usually  | Always |     |               |              |
| 8. a. If you have urgency, is it usually   |       | Mild         | Moderate | Severe |     |               |              |
| b. Does your urgency bother you?   | Never | Occasionally | Usually  | Always |     |               |              |
| SYMPTOM SCORE (1, 2a, 4a, 5, 6, 7a, 8a)  |       |              |          |        |     |               |              |
| BOTHER SCORE (2b, 4b, 7b, 8b)  |       |              |          |        |     |               |              |
| TOTAL SCORE (Symptom Score + Bother Score) =   |       |              |          |        |     |               |              |
| Total score ranges from 1 to 35. Likelihood of positive PST is 0% for scores 0-5, 57% for scores 6-9, 74% for scores 10-14, 79% for scores 15-19, and 91% for scores of 20 and higher. |       |              |          |        |     |               |              |
| ©2000 C. Lowell Parsons, Ph.D.   |       |              |          |        |     |               |              |

**Figure 22.1** The Pelvic Pain and Urgency/Frequency Patient Symptom (PUF) Scale is a self-administered questionnaire used to evaluate IC. Equal weight is given to symptoms of frequency, urgency, and pain.

### *Pelvic Pain and Urgency/Frequency Patient Symptom Scale*

The PUF Scale (see Figure 22.1) is a one-page, self-administered questionnaire that takes approximately 5 min to complete. Importantly, it gives equal weight to the symptoms of frequency, urgency, and pain. It also includes questions that address pain with sexual activity, a large but little-recognized part of the IC syndrome in both women and men. The PUF Scale quantifies both the presence of the symptoms and the degree to which the patient is bothered by them. The result is a single numeric score (maximum 35).

The data from a large validation study demonstrated a strong correlation between PUF score and likelihood of a positive PST. The PST was positive in 74% of patients who had

a PUF score of 10–14, 76% of those who scored 15–19, and 91% of those who scored 20 or higher. PUF Scale scores for all control subjects were less than 3.<sup>6</sup>

| POTASSIUM SENSITIVITY TEST  |  |  |
|---|--|--|
| Procedure   | Solution 1   | Solution 2   |
| <ol style="list-style-type: none"> <li>1. Ask the patient to rate baseline pain and urgency using the scales shown at right</li> <li>2. Place a small catheter in patient's bladder</li> <li>3. Slowly, over 1–2 minutes, instill Solution 1 into the bladder</li> <li>4. After 5 minutes, ask the patient to rate any pain and urgency on the scales</li> <li>5. Remove Solution 1 from the bladder</li> <li>6. Slowly, over 1–2 minutes, instill Solution 2 into the bladder</li> <li>7. After 5 minutes, ask the patient to rate any pain and urgency on the scales</li> <li>8. Remove Solution 2 from the bladder and rinse with 40 ml water</li> <li>9. Ask the patient to compare the two solutions using the questionnaire at right</li> </ol> | <div style="border: 1px solid black; padding: 5px; text-align: center;">Sterile water;<br/>40 ml</div> | <div style="border: 1px solid black; padding: 5px; text-align: center;">40 mEq<br/>KCl/100 ml<br/>water; 40 ml</div> |
| <p align="center"><b>Pain and Urgency Scales</b></p> <p><b>Pain</b></p> <p>None    Mild    Moderate    Severe</p> <p>0    1    2    3    4    5</p> <p><b>Urgency</b></p> <p>None    Mild    Moderate    Severe</p> <p>0    1    2    3    4    5</p> <p align="center"><b>Questionnaire</b></p> <p>1. Which solution is worse?</p> <p>... Solution 1</p> <p>... Solution 2</p> <p>... Neither</p> <p>2. Is the difference between the solutions:</p> <p>... Mild</p> <p>... Moderate</p> <p>... Severe</p>   |  |  |

**Figure 22.2** The potassium sensitivity test—specific instructions are delineated for this test.

### *Potassium Sensitivity Test*

In the PST (see Figures 22.2 and 22.3), the bladder is challenged with two separate intravesical solutions, water and potassium.<sup>16</sup> In response to a potassium challenge, a healthy individual with an effective urothelial permeability barrier suffers no urinary symptoms (urgency and/or pain). An individual who has an abnormally permeable epithelium, however, experiences urgency and/or pain as the instilled potassium passes through the urothelium and to the subepithelial tissues. Urgency and pain are abnormal responses that occur only if the patient's urothelium has a permeability defect that allows the potassium to reach the bladder interstitium.

The PST is gaining recognition as the most accurate method available for the diagnosis of IC. Currently, the medical literature contains significantly more published results of PST than of cystoscopy in patients with IC. The results of over 2000 PSTs have been published to date (Table 22.2). The data indicate that 79% of individuals with IC have a positive PST. False-positive PSTs are rare: 185/188 (98%) of healthy controls

have tested PST negative. Because of the intermittent nature of the symptoms of IC, however, an IC patient may test PST negative on any given day. For this reason, a positive PST can be taken as a definitive sign of IC, but a negative PST does not rule out the presence of IC.

### *Interstitial Cystitis Problem Index and Interstitial Cystitis Symptom Index*

O'Leary and coworkers developed the Interstitial Cystitis Problem Index (ICPI) and Interstitial Cystitis Symptom Index (ICSI) for use in quantitating the symptoms of IC.<sup>44</sup> A limitation of these questionnaires, however, is that they have only a single question concerning pain and they do not address pain other than bladder pain. In addition, they do not address the issue of pain flares associated with sexual activity nor do they address frequency.

## **Treatment**

Good control of the disease can be achieved in up to 85–90% of patients who have IC. An important principle of IC therapy is that treatment should not be withheld from a patient who has symptoms of IC but has tested negative on the PST. As discussed earlier, a negative PST does not rule out the presence of IC.

| PERMEABILITY STUDY  |   |   |                 |   |                         |             |                             |       |              |  |
|---|---|---|-----------------|---|-------------------------|-------------|-----------------------------|-------|--------------|--|
| Name: _____   |   |   |                 |   | Date: _____ Age: _____  |             |                             |       |              |  |
| URGENCY today: 0 1 2 3 4 5  |   |   |                 |   | PAIN today: 0 1 2 3 4 5 |             |                             |       |              |  |
| <b>SOLUTION A:</b>  |   |   |                 |   |                         |             |                             |       |              |  |
| 1. How much urgency to urinate do you have now compared to before the solution was placed? (Choose from 0 to 5)           |   |   |                 |   |                         |             |                             |       |              |  |
| none  | 0 | 1 | 2               | 3 | 4                       | 5           | severe                      | ONSET |              |  |
|   |   |   |                 |   |                         |             |                             | Grad  | Immed        |  |
| 2. How much pain in the bladder do you have now compared to before the solution was placed? (Choose from 0 to 5)          |   |   |                 |   |                         |             |                             |       |              |  |
| none  | 0 | 1 | 2               | 3 | 4                       | 5           | severe                      | ONSET |              |  |
|   |   |   |                 |   |                         |             |                             | Grad  | Immed        |  |
| <b>SOLUTION B:</b>  |   |   |                 |   |                         |             |                             |       |              |  |
| 1. How much urgency to urinate do you have now compared to before the solution was placed? (Choose from 0 to 5)           |   |   |                 |   |                         |             |                             |       |              |  |
| none  | 0 | 1 | 2               | 3 | 4                       | 5           | severe                      | ONSET |              |  |
|   |   |   |                 |   |                         |             |                             | Grad  | Immed        |  |
| 2. How much pain in the bladder do you have now compared to before the solution was placed? (Choose from 0 to 5)          |   |   |                 |   |                         |             |                             |       |              |  |
| none  | 0 | 1 | 2               | 3 | 4                       | 5           | severe                      | ONSET |              |  |
|   |   |   |                 |   |                         |             |                             | Grad  | Immed        |  |
| 3. If no pain noted in (2) above, have the patient void potassium and rate any perceived pain below: (Choose from 0 to 5) |   |   |                 |   |                         |             |                             |       |              |  |
| none  | 0 | 1 | 2               | 3 | 4                       | 5           | severe                      |       |              |  |
| <b>Which solution felt worse?</b>   |   |   |                 |   |                         |             |                             |       |              |  |
| Is A or B?  |   |   | A               |   | B                       |             | Neither (please circle one) |       |              |  |
|   |   |   | Mild            |   | Moderate                |             | Severe (please circle one)  |       |              |  |
| Vol. water IN:  |   |   | Vol. water OUT: |   |                         | Vol. KO IN: |                             |       | Vol. KO OUT: |  |

**Figure 22.3** This potassium sensitivity test questionnaire quantifies urgency and pain associated with instilled potassium solution. Solution 1 is 40 ml of sterile water and solution 2 is 40 ml of a solution of 40 mEq KCl/100 ml water. This scale also evaluates the

## pain during voiding of the potassium solution.

### *Heparinoid therapy*

Heparinoid therapy, where available, is the treatment of choice for IC. The cornerstone of treatment for IC is the oral drug pentosan polysulfate sodium (PPS; Elmiron®),<sup>45,46</sup> a compound that is similar in structure to the GAGs at the bladder surface. PPS is believed to aid in repair or restoration of the bladder epithelium.<sup>45</sup> The recommended dose of PPS is 100 mg three times per day, but our experience (especially in men) shows 600 mg/day or even 900 mg/day doses are more effective. A new study shows that the longer PPS is taken, the more effective it is.<sup>47</sup> In general, PPS must be tried for at least 12 months before its effectiveness is evaluated.

Ideally, PPS is used as part of a multimodal oral treatment regimen that includes the antihistamine hydroxyzine to combat any allergies that may aggravate IC. In some cases the use of an antidepressant such as amitriptyline is warranted to reverse the neural activation in the bladder (Table 22.3).

Particularly in severe IC, intravesical heparin can be used either alone or in combination with PPS (Table 22.4).<sup>48</sup> In a typical case, we combine a regimen of intravesical heparin therapy with concomitant oral PPS. The patient is directed to administer intravesical heparin 40,000 IU in 10 ml 1% lidocaine and 3 ml of sodium bicarbonate 1–2 times daily. Once a patient is responding well, the intravesical heparin can be slowly tapered and then

**Table 22.2** *Reported results of testing for epithelial dysfunction in patients with lower urinary tract symptoms of urgency/frequency and/or pelvic pain*

|  | Patients                    |                             | Controls                    |                             |
|--|-----------------------------|-----------------------------|-----------------------------|-----------------------------|
|  | UCSD                        | Non-UCSD                    | UCSD                        | Non-UCSD                    |
| Senior author and year of report (reference) | No. positive/No. tested (%) | No. positive/No. tested (%) | No. positive/No. tested (%) | No. positive/No. tested (%) |
| Parsons 1994 <sup>28</sup>                   | 23/33 (70%)                 |                             | 1/22 (5%)                   |                             |
| Payne 1996 <sup>35</sup>                     |                             | 18/20 (90%)                 |                             | —                           |
| Parsons 1998 <sup>16</sup>                   | 174/231 (75%)               |                             | 2/71 (3%)                   |                             |
| Chambers 1999 <sup>36</sup>                  |                             | 24/39 (62%)                 |                             | —                           |
| Teichman 1999 <sup>37</sup>                  |                             | 23/38 (61%)                 |                             | —                           |
| Parsons 2001 <sup>7</sup>                    | 362/466 (78%)               |                             | 0/42 (0)                    |                             |
| Chen 2001 <sup>38</sup>                      |                             | 21/23 (91%)                 |                             | —                           |
| Daha 2001 <sup>39</sup>                      |                             | 12/13 (92%)                 |                             | —                           |
| Forrest 2001 <sup>40</sup>                   |                             | 7/8 (88%)                   |                             | —                           |
| Kuo 2001 <sup>41</sup>                       |                             | 40/40 (100%)                |                             | —                           |
| Grégoire 2002 <sup>42</sup>                  |                             | 105/128 (82%)               |                             | —                           |
| Parsons 2002 <sup>43</sup>                   | 24/30 (80%)                 | 278/347 (80%)               | —                           |                             |
| Parsons 2002 <sup>14</sup>                   | 37/44 (84%)                 |                             | —                           |                             |

|                            |                           |               |                      |          |
|----------------------------|---------------------------|---------------|----------------------|----------|
| Parsons 2002 <sup>6</sup>  | 263/344 (79%)             |               | 0/6 (0)              |          |
| Parsons 2002 <sup>a4</sup> |                           | 197/244 (81%) |                      | 0/47 (0) |
| Subtotals                  | 883/1138(78%)             | 725/900 (81%) | 3/141 (2%)           | 0/47 (0) |
| <b>Totals</b>              | Patients: 1608/2038 (79%) |               | Controls: 3/188 (2%) |          |

<sup>a</sup>Data collated by Dr Parsons from tests performed by gynecologists at five US centers other than University of California, San Diego (UCSD).

discontinued. Lower doses of heparin can also be helpful. Heparin administered in a dose of 10,000 units daily by itself is effective.<sup>48</sup>

Because it takes time for up-regulated bladder nerves to deactivate, urgency and pain can persist in an IC patient after the epithelium has been restored. In a patient who has mild-to-moderate disease, the results of heparinoid therapy should be judged only after at least 1 year of treatment. In patients with severe IC, the assessment should be made only after at least 2 years of treatment.

Other modalities can be used, as described below, if heparinoid therapy is not available.

**Table 22.3** *Oral medications for IC treatment*

| Medication             | Dosage            |
|------------------------|-------------------|
| PolyCitra <sup>a</sup> | 10 mg twice daily |
| Amitriptyline          | 25–75 mg/day      |
| Hydroxyzine            | 10–50 mg/day      |

<sup>a</sup>PolyCitra is trade name for a urinary alkalinizing preparation containing potassium citrate

**Table 22.4** *Intravesical heparin for treatment of IC*

| Purpose                              | How often               | Dosage   |
|--------------------------------------|-------------------------|--|
| Chronic therapy                      | Daily                   | Heparin 10,000–40,000 units in 10 ml water   |
| Maintenance therapy                  | Monday-Wednesday-Friday | Heparin 10,000–40,000 units in 10 ml water   |
| Immediate relief of pain and urgency | Once or twice daily     | Heparin 10,000–40,000 units in 8 ml lidocaine 1% <sup>a</sup> and 3 ml 8.4% sodium bicarbonate |

<sup>a</sup>Lidocaine may be doubled to 2% if no relief.

### *Intravesical therapies*

In 2002, we obtained promising results in a preliminary study of an intravesical solution for the immediate and sustained relief of the symptoms of urgency and pain in patients with IC (unpublished data). The solution contains 40,000 units of heparin or 100 mg PPS, 80 mg of lidocaine, and 3 ml of 8.4% sodium bicarbonate in a volume of 15 ml of total fluid. The presence of the sodium bicarbonate, which increases the absorption of the lidocaine, is the principal difference between our therapeutic solution and similar solutions that have been tried. In our preliminary study, 31 of 40 patients (78%) experienced significant immediate relief of IC symptoms. Sustained pain relief was obtained in 85% of the patients who used the solution 3–7 times weekly for 2 weeks or

more. If further studies confirm these promising initial data, this intravesical solution is the first treatment that offers immediate relief of the pain and urgency of IC.

Dimethyl sulfoxide (DMSO) treatment can be useful in weekly intravesical instillations for 6–8 weeks (Table 22.5). DMSO was approved for IC in 1977 on the basis of data from uncontrolled trials. Approximately 50% of patients treated with DMSO will benefit from this therapy. Alternatively, intravesical instillations of hyaluronic acid may be helpful to some patients. Hyaluronic acid is a GAG marketed in Canada as Cystistat®.

### *Cystoscopy under anesthesia*

Cystoscopy under anesthesia can be performed as a therapeutic measure in cases of severe IC. This procedure has been a mainstay of therapy since Bumpus reported the effects of bladder hydrodistention in improving the symptoms of IC.<sup>49</sup> Hydrodistention probably works by causing a neuropraxis.

The procedure must be performed under anesthesia because a painful bladder cannot be dilated without it. The bladder is filled to 80 cmH<sub>2</sub>O pressure, with manual compression of the urethra to prevent leakage during the filling phase. Once the bladder is full, the water is left in for 2–3 min and then the bladder emptied. This is when glomerulations appear.

In approximately 60% of patients, hydrodistention produces an improvement in symptoms that may last for 6–10 months. Most patients have an intense symptom flare for several days or weeks after the procedure before they enter remission. Biopsy has no role in IC diagnosis. It should be performed only to rule out other disease, and only after the hydrodistention to avoid bladder rupture.

### **Dietary management**

Dietary management can be of benefit to patients who have IC. In general, we advise our IC patients to avoid potassium-rich foods; the four foods that our patients associate most often with aggravation of symptoms are citrus fruits, tomatoes, chocolate, and coffee. All of these are extremely high in potassium, having a composition of 99% potassium and 1% sodium. We also advise our patients to avoid spicy foods or foods flavored with peppers. In addition, we often find it helpful for our IC patients to use either PolyCitra-K® crystals, one packet twice a day, or Urocit-K® 10 mEq twice a day as a chelating agent in urine. Finally, we encourage our patients to try over-the-counter ‘nutriceuticals’ such as Prelief in the management of IC, although there are no clinical data to substantiate their benefit.

**Table 22.5** *Intravesical dimethyl sulfoxide (DMSO) for treatment of IC*

| Purpose         | DMSO dosage                         |
|-----------------|-------------------------------------|
| Initially       | 50 ml weekly for 8 weeks            |
| For maintenance | 50 ml every 2 weeks for 3–12 months |

*Neurotoxins*

Resiniferatoxin and capsaicin are being studied and may be shown to be beneficial in the treatment of IC.

*Neurostimulators*

Implantable neurostimulators have been reported to have some benefit in patients who have severe IC.<sup>50</sup> These may also become useful in patients with disease that is refractory to more conservative medical management.

*Surgery*

Approximately 2% of the IC patients we have seen at the University of California, San Diego (UCSD), have ultimately undergone surgery for their disease. Surgery is considered in cases of severe disease that is refractory to all other treatment.

Cystectomy and diversion (see Chapters 37 and 51) is the mainstay of surgical therapy for patients with 'endstage bladder.' In general, the procedure can provide relief of symptoms for those IC patients who have classic bladder pain that is associated with filling and that is relieved or partially relieved by emptying, urinary frequency, and urgency, and the usual stigmata of IC upon cystoscopy under anesthesia. It is less likely that cystectomy and diversion will alleviate pain in patients who have severe pelvic pain that is not associated with classic findings of IC and particularly is not exacerbated by bladder filling.

In 5% of patients, pelvic pain will present after the procedure; 40–50% of patients will develop pouch pain 6–36 months after continent diversion. To manage their pouch pain successfully, patients can be instructed to instill 10,000 units of heparin in 10 ml water into the pouch after each catheterization. To prevent the development of pouch pain in our patients who undergo continent diversion, we routinely prescribe a regimen of oral Elmiron (PPS) 300 mg daily along with daily intravesical heparin.

The use of another surgical procedure, bladder augmentation, for IC is based on the erroneous concept that individuals with IC void frequently because they have small bladders. The reverse is actually true: IC patients have sensory urgency, void frequently, and subsequently develop a small bladder. For this reason, attempts to augment the bladder with a patch of bowel are likely to fail. After the procedure, patients will have perhaps a large bladder capacity and will have more difficulty emptying (usually requiring intermittent catheterization), but still retain all their sensory urgency and pain.<sup>51</sup>

**Conclusions**

The disease known as 'IC' appears to be part of a larger disorder that arises from a urothelial dysfunction and can affect tissues throughout the lower urinary tract. This disorder can be called lower urinary dysfunctional epithelium (LUDE). The PST is an effective tool for detection of this disease. The PUF Scale, a new symptom questionnaire, can be useful in both screening and diagnosis. Detection of the disease is important,

because up to 85–90% of cases can be treated effectively using a three-part treatment plan based on PPS.

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## 23

# Vesicovaginal fistula repairs\*

Michael J Sebesta and R Duane Cespedes

### Introduction

Vesicovaginal fistula has been a recognized entity for centuries. The ancient Egyptians described Vesicovaginal fistula in the Ebers papyrus; unfortunately, the treatment of fistulas was greeted with almost certain failure during those times. Likewise, attempts to treat fistulas during the Renaissance period were uniformly unsuccessful.<sup>1</sup> Management of such fistulas was largely expectant until the development of modern medical techniques.

Sims was the first to describe the routine closure of Vesicovaginal fistulas, although it often required multiple attempts. His techniques were improved and included nonvaginal approaches such as Trendelenburg's transabdominal approach and Leguen's transvesical approach.<sup>2</sup> Martius and Garlock popularized tissue interposition grafts in the 1920s with some success. One of the last but perhaps simplest advancement was to include routine catheter drainage. Modern physicians continue to improve and perfect the surgical treatment of Vesicovaginal fistula; however, little has been written about the minimally invasive treatment of Vesicovaginal fistula.

### Etiology

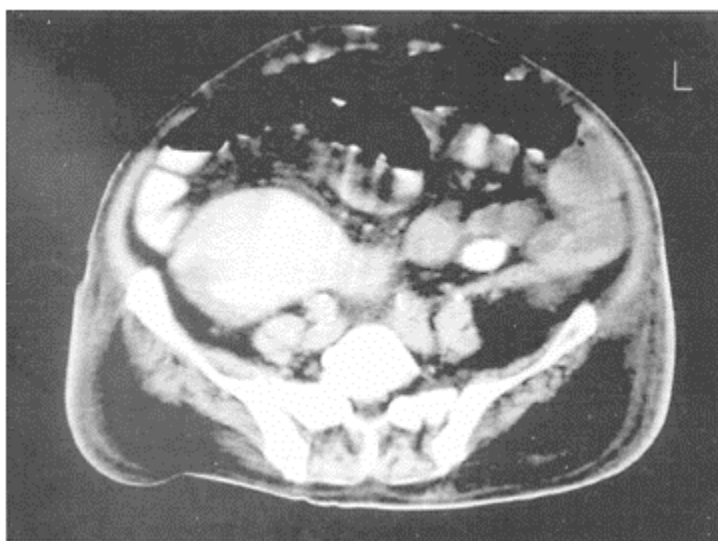
Routine hysterectomy is the most common cause of vesicovaginal fistula in developed countries.<sup>3</sup> Fistula formation typically occurs by the incorporation of vaginal tissue into an unidentified bladder injury. This results in tissue necrosis and fibrosis, ultimately leading to an epithelial or mucosal lined tract. It is also possible that partial-thickness bladder injuries can become fistulas by localized infections or postoperative urinary retention resulting in urinary leakage and fistula formation. Uncommon etiologies of fistula formation include malignancy, radiation, gastrointestinal surgery, inflammatory bowel disease, and tuberculosis. Vaginal and uterine foreign bodies have been reported to cause Vesicovaginal fistulas. Treatment of vaginal condylomata with the carbon dioxide laser has also been reported to cause Vesicovaginal fistulas.<sup>4</sup> Finally, diseases causing

\* The opinions expressed herein are those of the authors and do not reflect those of the Department of Defense, the U.S. Army or the U.S. Air Force.

vasculitis of the bladder wall may rarely induce fistula formation. Factors which may contribute to post-hysterectomy fistula formation include prior Caesarean section, uterine disease, and prior pelvic radiation therapy.<sup>5</sup> The incidence of fistula after hysterectomy is reported to be 0.1–0.2%.<sup>6</sup>

### Clinical features

Continuous drainage of urine per vagina is the cardinal sign of Vesicovaginal fistula. It is typically diagnosed days to weeks after the initial insult. Patients may present during initial hospitalization with hematuria, flank pain, pain out of proportion to the procedure performed, or prolonged ileus<sup>7</sup> (Figure 23.1). If a large fistula tract is present, there will be continuous incontinence. In cases of a small fistula, patients may demonstrate a stress incontinence-like syndrome such that urine is commonly expelled from the vagina when coughing. This situation may cause a diagnostic dilemma. This is especially true in women who received pelvic radiation in the past because these fistulas may take up to 20 years after initial therapy to develop. A careful evaluation is needed in these patients to avoid performing an unnecessary incontinence procedure. Vaginal discharges unrelated to a Vesicovaginal fistula may have multiple causes. Vaginal infections are a common cause of clear vaginal discharge and a slight discharge is common postoperatively and is usually related to the healing process; however, there are other etiologies. Peritoneal fluid may leak through a sinus tract in the vaginal cuff after hysterectomy (post-hysterectomy pseudo-incontinence).<sup>8</sup> Ginsburg has previously described



**Figure 23.1** CT scan of a patient who complained of fevers, vaginal leaking,

and flank pain. A large fluid collection can be seen in the right retroperitoneum, with a prominent contrast layer. The patient was found at surgery to have a combined ureteral and bladder injury.

five patients with this condition: after vaginal cuff revision, all five patients were cured.<sup>9</sup> Fallopian tube drainage and lymphatic drainage may also cause clear vaginal discharge. Finally, one may observe urge or stress incontinence, ectopic ureter, ureterovaginal fistula, or ureteroutero fistula.

### Diagnosis

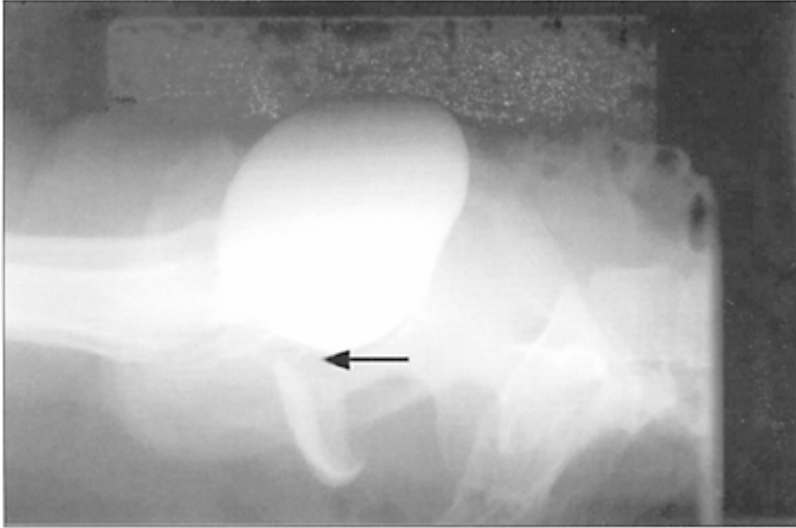
A thorough history is essential in diagnosis of a vesicovaginal fistula: in particular, the physician should pay attention to previous surgical and obstetric history. Prolonged labor through a narrow pelvis is known to cause many vesicovaginal fistulas in the developing world and is the occasional etiology in the developed world. The time of onset and duration of symptoms should be noted. One should determine whether leakage is continuous or intermittent, as this may help differentiate between a vesicovaginal fistula and a ureterovaginal fistula. The amount of leakage may help predict a large vs small fistula. Whether the patient voids small amounts or at all is not usually helpful unless both ureters are injured, which is usually easily diagnosed. A history of urinary tract infection, urgency, or stress incontinence symptoms should be noted.

Physical examination is crucial in the diagnosis of a fistula. A thorough vaginal examination for a fistula tract is helpful but is rarely sufficient to determine the site of leakage, the size of the fistula, or number of fistulae. The vaginal size, mucosal quality, and presence of induration should also be noted, factors all important in determining the patient's subsequent surgical options.

Post-hysterectomy fistulas are typically located at the vaginal cuff, with pooling of urine in the vaginal fornices. A very large fistula tract may be identified visually at the cuff, but this is rare, and usually other tests are required. A dye test using oral phenazopyridine (Pyridium) is useful in conjunction with placement of a vaginal tampon. The appearance of orange staining at the proximal end of the tampon will confirm a fistula. The placement of methylene blue into the bladder is also commonly used. Neither of these tests localize the fistula, however, and only confirm that a vesicovaginal fistula is present. Localization almost always requires cystoscopy. Cystoscopy allows the examiner to localize the fistula (using a finger in the vagina to confirm), verify the number of fistulae present, and determine its proximity to other structures, such as the ureter. All of this information is required for surgical management decisions. Of note, a bladder biopsy, either transvesical or transurethral, should be considered in patients with previous pelvic malignancies, especially if radiation was given.

Radiographic studies can help in the diagnosis and surgical planning of fistula treatment. The ureters should also be evaluated, given an approximate 5% chance of

concomitant ureterovaginal fistula. This may be accomplished using an intravenous pyelogram (IVP). An IVP also allows one to visualize pooling of contrast in the proximal vagina in the cystogram phase (Figure 23.2). Retrograde pyelography, however, provides greater



**Figure 23.2** Lateral cystogram of a patient who complained of vaginal leakage after a hysterectomy. In the supine position, the contrast is pooling in the proximal vagina and the fistula tract can be seen at the arrow.

accuracy in diagnosing ureterovaginal fistula. A voiding cystourethrogram (VCUG) may aid in localizing a fistula and demonstrating other lower urinary tract anomalies, which may influence reconstruction decisions. Some investigators recommend vaginography to demonstrate irregular fistulous tracts, although these are difficult to perform and interpret.<sup>10</sup>

Fluorourodynamics may be helpful in preoperative planning by confirming concomitant detrusor or sphincter ic dysfunction. A small series by Hilton demonstrates a 47% incidence of stress urinary incontinence, 44% incidence of detrusor instability, and 17% poor detrusor compliance.<sup>11</sup>

### **Surgical treatment**

A mature fistula provides the best opportunity for successful surgical intervention. When operating in a nonirradiated field without persistent carcinoma, success rates as high as

85–90% may be achieved. Multiple factors affect the success rate of operative intervention, including etiology of the fistula, presence of necrotic tissues, and the surgeon's experience. In addition, the best success rates are achieved with the initial surgery.<sup>12</sup> Failure rates are generally proportional to the number of operative interventions needed to treat the fistula.

In the past, waiting periods of 3–6 months were advocated prior to embarking upon fistula repair.<sup>13,14</sup> This dictum has become controversial, as several authors have reported very good success rates with early repair.<sup>15–17</sup> Current recommendations are that immediate fistula repair may be undertaken if recognized within 72 hours. Fistulas recognized later in the postoperative course should be carefully considered as fistulas can certainly be successfully treated prior to 3 months; however, it is important to keep in mind the important determinants of successful fistula repair, such as prior radiation treatment, current infections, large fistula size, multiple fistulae, poor tissue quality, and poor overall patient health and nutrition.<sup>18,19</sup> Patients with these adverse prognostic conditions should probably wait 3 months to let the tract mature and improve the adverse conditions.

### *Preoperative preparation*

Many authors recommend vaginal douches with antiseptic agents the evening prior to and the morning of surgery. As some of these patients will have recurrent urinary tract infections, prophylactic broad-spectrum intravenous antibiotics in the perioperative period (prior to incision and 24–48 hours postoperatively) are administered. Continued low-dose prophylactic antibiotics are continued while the catheter is in place. Patients with poor-quality vaginal tissues should receive topical estrogen replacement for 4–6 weeks postoperatively.<sup>20</sup>

### *Surgical approaches*

Surgical approaches used for vesicovaginal fistulas include minimally invasive, vaginal, combined vaginal and abdominal, and abdominal. The approach used relies upon several factors, including location in relation to the vaginal apex, tissue quality, and experience.

Endoscopic approaches can be used in patients with a single, small fistula. The procedure of 'roughing up' the fistula with a ureteral catheter and placing a Foley catheter can be performed in the office with minimal morbidity. Of the true surgical procedures, the vaginal approach is the quickest and has minimal associated morbidity. Unfortunately, this approach can rarely be used in the posthysterectomy patient due to fixation of the vaginal apex and concomitant rectocele and perineorrhaphy which reduce exposure. Transvaginal surgery is useful for bladder injuries noted during the course of a vaginal hysterectomy. Additionally, it is a poor approach when the fistula is in close proximity to the ureters.

The abdominal approach should be used in patients with multiple, large, or poorly visualized fistulas and in patients with a narrow immobile vagina. Additionally, this approach is needed in fistula located close to the ureteral orifice. Of note, there are two separate abdominal approaches possible.

No matter which approach is taken, a few caveats are important. At the end of the procedure, the closure must be perfectly watertight. Any leakage will impede healing and may result in a failure. The suture lines of the bladder and vagina should not directly overlap. In cases of overlapping suture lines, one should interpose tissue of some type.

### Endoscopic management

Fistulas may be approached transurethraly. This provides a working environment familiar to the urologist and minimal patient morbidity. Transurethral fulguration has been shown to be effective in treating small fistulas. Falk and Orkin reported in 1957 that 8 of 10 fistulas were successfully managed with cystoscopic electrocoagulation.<sup>21</sup> The failures in this group were women with fistulas greater than 3 mm in diameter. A more recent experience by Kursh and colleagues revealed similar results. These investigators treated fistulas 2–3 mm in size. A Bugbee electrocautery was used to fulgurate the tract either cystoscopically or through the vagina. The bladder was decompressed for 14–28 days with a large-bore indwelling catheter. Ten of 14 patients experienced complete resolution of the fistula.<sup>22</sup>

The probable mechanism by which these treatments work is that fulguration destroys the epithelial lining of this tract. This promotes side-to-side healing of the vesical and vaginal mucosa as long as good tissue exists and adequate drainage is maintained. These procedures are only indicated for small fistulas and are futile in larger fistulas. In addition, low current should be applied to confine the area of destruction to the epithelial lining of the tract. In addition to electrocoagulation, laser ‘welding’ of the fistula tract may be used.<sup>23</sup>

Electrocoagulation used in conjunction with tissue sealants may provide a method for treatment of larger fistulas. Morita and Tokue report success in treating a 5 mm tract using electrofulguration of the fistulous tract with concomitant use of fibrin sealant in the tract. The tract was then closed with intravesical and intravaginal submucosal injections of bovine collagen.<sup>24</sup> While experience with this technique for vesicovaginal fistula is limited and our own experience in 3 patients was unsuccessful, it is reasonable to attempt this as a first-line approach in small, easily visualized fistulas.

Transurethral suture cystorrhaphy is another minimally invasive technique used to close the fistula. This technique allows the fulgurated edges of a wide fistula tract to be kept in close approximation during healing. McKay reported his experience with 5 patients receiving such a closure.<sup>25</sup> His initial experience with pure transurethral techniques using a 32F Amplatz sheath and an offset 12 mm operating laparoscope were largely unsuccessful as access to the bladder and knot tying were very difficult. The author later altered his approach by using a separate suprapubic tract for visual access and using the urethra for working instrument access. Specifically, a 15F arthroscope is passed through a 16F suprapubic cystotomy. A 21F cystoscope is used to fulgurate the tract with a Bugbee electrocautery. A 30F Amplatz renal fascial dilator with a 32F sheath (ARD 075230, Cook Urological, Inc., Spencer, Indiana) is passed through the urethra without preliminary dilation. Leakage is prevented with a rubber cap (Richard Wolfe, 5–6 mm type C seal—89.03 GY) placed over the end of Amplatz sheath. Four 2–0 Vicryl sutures on a CT-2 needle are passed with a self-righting laparoscopic needle driver. The suture(s) are passed transversely through the edges of the fistula to ensure a watertight closure.



With a follow-up of 74 months, 4 of 5 patients remain cured and the patient who failed went on to transabdominal repair.

### **Laparoscopic approach**

There are few reports describing or supporting the use of laparoscopic techniques in the treatment of vesicovaginal fistula. No large studies exist to demonstrate the efficacy of this technique. This is probably due to the small incidence of vesicovaginal fistula and the minimal morbidity associated with endoscopic and transvaginal repairs. The literature does contain several case reports of repairs containing a limited number of patients. Most repairs were done on complex fistulas in which the surgeon considered repair via laparotomy. Unfortunately, patients who received one or more previous attempts at a repair will have extensive scarring, making a laparoscopic approach difficult. The best candidates are likely to be patients who cannot be repaired transvaginally and who have relatively simple fistulas.

For this procedure, the patient is placed in a low lithotomy position and cystoscopy is performed. Both ureters are identified and stented. The fistula tract is identified and intubated with a ureteral stent. These maneuvers are important because they allow for intraoperative identification of these structures. A 10 mm infraumbilical port is placed using either the Hasson technique or a Veress needle. A 12 mm port is placed in the left paramedian area while a 5 mm port is placed in the right paramedian area.<sup>26</sup>

An EEA sizer elevates the vaginal apex and facilitates dissection. The vesicovaginal space is dissected using both scissor and blunt dissection. Filling the bladder with 300 ml of fluid assists in the dissection. Alternatively, the dissection may be performed with the CO<sub>2</sub> laser and hydrodissection.<sup>27</sup> Identification of the intrafistular stent confirms entry into the fistula. The tract is then excised and dissection continued 2 cm distally to mobilize the vagina and bladder edges. Excision may be done either sharply or with a laser.

Both vaginal and bladder closures should be performed in separate layers. The vaginal wall opening is closed with one layer of interrupted polyglactin suture. The bladder may be repaired in one layer with interrupted 1-0 Endoknot Vicryl sutures (Ethicon Endo-Surgery, Inc., Sommerville, New Jersey) using extracorporeal knot tying. The entire vesicovaginal space and fistula area should be examined for hemostasis.

Tissue interposition may be performed with a peritoneal flap. A peritoneal flap may be obtained superior and lateral to the bladder dome close to the round ligament with diversion toward the bladder base. It may be secured in place with interrupted Vicryl sutures. Alternatively, omentum may be mobilized for interposition. This removes the necessity for vaginal closure; however, closure should still be performed if able to do so.<sup>28</sup> The omental flap, based on the gastroepiploic vessels, is dissected free with the use of Endo-GIA 30 staples. It is inserted between the vagina and bladder. The flap is then stapled to the vagina and parietal peritoneum with the Endo-Hernia (4.8 mm cartridge) stapler.

There are only limited data on laparoscopic treatment of vesicovaginal fistula. Most case reports demonstrate success in a small number of patients. This technique does, however, allow one to follow the principles outlined by Moir for successful fistula repair:

1. suitable equipment and lighting

2. adequate exposure during the operation
3. excision of fibrous tissue from the edges of the fistula
4. approximation of edges without tension
5. use of suitable suture material
6. efficient postoperative drainage.<sup>29</sup>

All of these conditions may be met by laparoscopic repair. In addition, it may be performed if one considers performing a concomitant laparoscopic nephrectomy or other laparoscopic procedure.<sup>30</sup>

### **Vaginal approach**

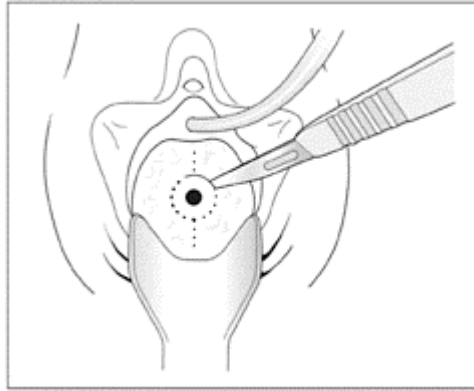
The vaginal approach relies upon creation of an anterior vaginal wall mucosal flap. Tension-free closure is achieved by use of a long-acting (polyglycolic acid or polydioxanone) suture and use of overlapping suture lines. Interposition flaps should be liberally used as needed.

Urinary drainage should be maintained through a suprapubic catheter and supplemented by a urethral catheter.<sup>31</sup> With fistulas in close proximity to the ureteral orifices, ureteral catheterization and intraoperative visualization of the ureters should be done. Tissue mobilization provides optimal visualization, and relaxing incisions should be placed as needed to supplement visualization.

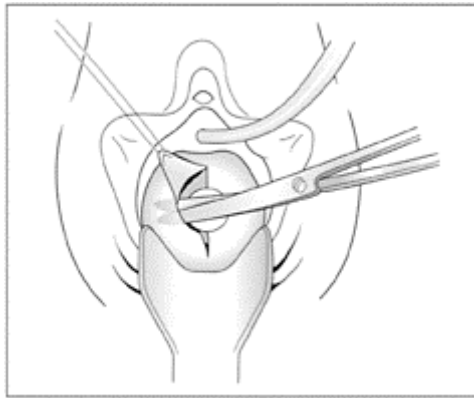
To assist dissection, vaginal retraction is obtained with a self-retaining retractor and a small balloon catheter in the fistula tract. A 'U'- or 'J'-shaped vaginal mucosal incision, incorporating the base of the fistula, can be utilized for large fistulas. The flap is usually oriented anteriorly for fistulas located at the cuff. Posterior flaps or circular circumscription, however, may be utilized in smaller fistulas. Note that the tract should be circumscribed but not widely excised. The peripheral tissues provide buttressing for closure and wide excision may result in a large tissue defect, which creates tension on the closure and may cause the repair to fail.

Complete mobilization of the vaginal wall away from the edges of the fistulous tract is performed and the vaginal wall opposite the flap is excised to allow advancement of the vaginal flap beyond the fistula's repair site once the fistula is closed. Debridement of the edges may be required to avoid a bunching effect on the tissue with closure (Figures 23.3 and 23.4). The fistula tract is closed with running 2-0 polyglycolic suture incorporating the 'freshened' fistula tract and full thickness of bladder wall (Figure 23.5). The bites should be close enough to ensure a watertight closure. If sufficient tissue exists, a second layer, vertically oriented to the first, is made using the perivesical tissue. Advancing the vaginal wall over the tract using absorbable suture creates a third and final layer.

Loose vaginal packing is placed and catheter drainage maintained. It is critically important to have both a Foley catheter and suprapubic drain for at least the first week. We

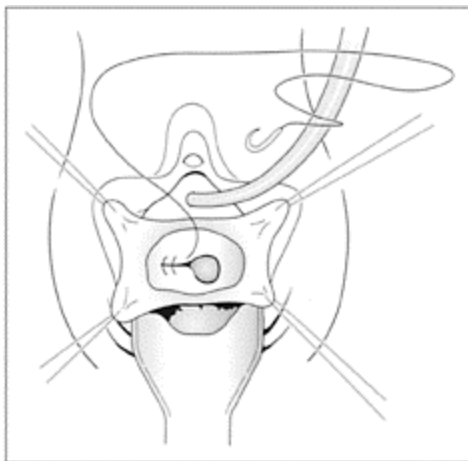


**Figure 23.3** The fistula is circumscribed and the mucosa incised at the dotted lines.



**Figure 23.4** Dissection of the vaginal flaps to allow easy closure of the fistula and the subsequent layers.

have been consulted to perform repeat repairs due to clot retention and/or Foley catheter kinking, causing rupture of the repair and treatment failure. A Martius flap may be used in complex redo cases but this is rarely needed unless the tissue has been radiated. A Martius interposition graft uses the fibrofatty tissue of the labia majora and is usually based on its superior blood supply for fistula repairs<sup>32</sup> (Figure 23.6). The graft is mobilized and then tunneled under the vaginal wall from the labia to the vaginal incision. It is sutured on the far side of the fistula with multiple fine absorbable suture. It is important not to injure the blood supply. The vaginal mucosa is closed over the site and the Penrose drain is left in place.



**Figure 23.5** The fistula tract is closed full thickness to include the mucosa and bladder muscle. A second layer of perivesical tissue or even pubocervical fascia can be laid over this layer prior to closing the vaginal mucosa.

Other sources of flap material include peritoneum, and gracilis, but again, are rarely needed. Poor operative candidates may undergo the Latzko technique of proximal vaginal fistula repair. In this technique, the vaginal epithelium surrounding the fistula is excised. A colpocleisis is then performed with several layers of absorbable sutures placed from anterior to posterior vaginal wall. This effectively obliterates the proximal vagina. This technique does not require fistula tract excision and, likewise, there is no need for ureteral reimplantation. There is a compromise of vaginal length but no effect on sexual activity.

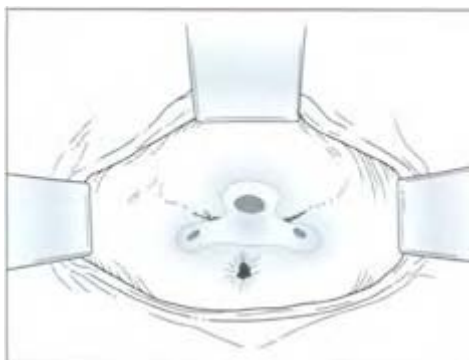
### Transvesical approach

The transvesical approach is the least morbid of the vesicovaginal fistula procedures which require an abdominal incision. Generally, any vesicovaginal fistula can be closed using this approach; however, since interposition grafts are difficult to place with this approach, an O'Connor approach (see Abdominal approach section) may be a better choice.

A Pfannenstiel incision is made and the anterior bladder wall cleared of adipose tissue. A 4–5 cm incision is made horizontally in the anterior wall of the fluid-filled bladder. The horizontal incision ensures that undesired bladder tears do not injure the bladder neck. A Judd-Mason or other suitable retractor is placed in the bladder and the fistula tract identified (Figure 23.7). An EEA sizer is placed



**Figure 23.6** Preparation of a Martius graft based on the superior blood supply. The fat pad is relatively small in this thin individual; however, the graft is invariably long enough if done correctly.



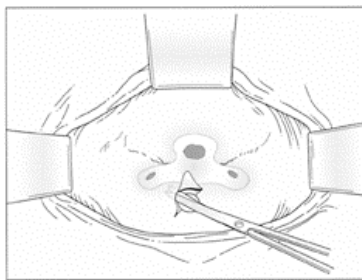
**Figure 23.7** The fistula tract, located just behind the trigone in most cases, can be easily approached using the transvesical approach.

in the vagina to bring the fistula upwards and to allow a hard surface for circumscription and dissection of the layers (Figure 23.8). The vaginal layer is isolated and then closed with a running 2-0 Vicryl suture (Figure 23.9). A watertight mucosal closure is then performed using a 3-0 absorbable suture (Figure 23.10). An SP tube is placed and the bladder and abdomen closed in the usual manner. A Foley catheter is always left in place in addition to the SP (suprapubic) tube.

Our experience using this approach in 18 patients with over 1 year follow-up has been excellent: only 1 patient had a slight persistent leak at 2 weeks, and by 3 weeks all patients were cured. Of these 18 patients, 4 were reoperative cases.

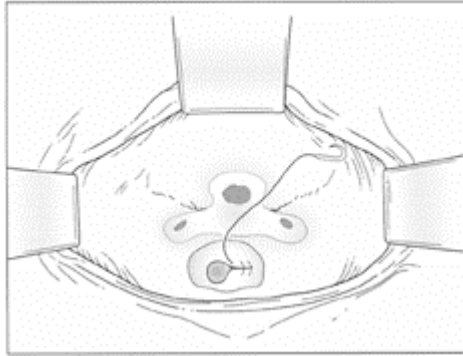
### Abdominal approach

All bladder fistulas may be approached abdominally. This is the preferred approach in patients requiring bladder



**Figure 23.8** The fistula tract is circumscribed and the mucosa

dissected free for approximately 1–2 cm around the fistula. It is important to avoid dissection around the ureteral meatus.

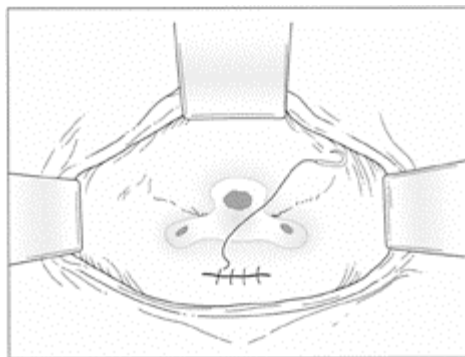


**Figure 23.9** The vaginal wall is closed with a running absorbable suture, ensuring that there is no tension on the closure.

augmentation or ureteral reimplantation. Indications for an abdominal approach include:

1. inadequate exposure because of a high or retracted fistula in a narrow vagina
2. proximity of the fistula to the vagina
3. associated pelvic pathology
4. multiple fistulas.<sup>33</sup>

O'Connor and associates reported early work with abdominal transvesical repair of vesicovaginal fistula. This technique requires placement of ureteral catheters to localize the ureteral orifices. An abdominal incision (midline or Pfannenstiel) is performed and the bladder bisected



**Figure 23.10** The mucosa is closed with a running absorbable suture—a watertight closure is imperative to avoid recurrences.

starting in the mid bladder all the way around through the level of the fistula (Figure 23.11). The required bladder and vaginal mobilization ensures that the vagina and bladder are separated at the level of the fistula. The fistulous tract is dissected, completely excised, and closed with a running absorbable suture (Figure 23.12). The bladder layers (mucosa and muscle) are closed separately, starting with a watertight closure of the mucosa with 3–0 absorbable suture. The muscle is then closed with a running 1–0 Vicryl suture (Figure 23.13). Although theoretically this case can be performed extraperitoneally, rarely is this possible since in most cases the prior hysterectomy causes severe scarring and downward displacement of the peritoneal contents. Therefore, this technique is most expeditiously performed intraperitoneally. In addition, the intraperitoneal approach facilitates omental harvest for interposition. When using omentum, it is secured between the bladder and vagina with 3–0 polyglycolic acid sutures. The bivalved bladder is also readily available for augmentation if needed.

### Complicated vesicovaginal fistulas

Complicated vesicovaginal fistulas are defined as being greater than 3 cm in greatest diameter, reoccurring after prior closure attempt, associated with prior radiation, associated with malignancy, or involving the bladder neck, urethra, or trigone.

Reconstructive techniques using a variety of interpositional tissues have been described to deal with such fistulas. Fibrofatty labial interposition tissues, anterior/posterior flaps, and myocutaneous flaps have all been described as adjuncts to repair.

Gracilis flaps provide an easy interposition material for fistula. The flap should be isolated from an incision over





**Figure 23.11** The bladder has been bisected through the level of the fistula, ensuring that the bladder and vagina are separated at the site of the fistula.



**Figure 23.12** The vaginal portion of the fistula is resected and then closed with a running absorbable suture. This step is important even if an interpositional graft will be used.

the medial thigh from the medial condyle of the femur to the inferior border of the pubic symphysis. The distal tendinous insertion is identified and transected. A tunnel from the thigh to vagina is developed and the flap placed through this tunnel. It is affixed over the closed fistula site. If vaginal mucosa cannot be closed over the flap, it may be left open to re-epithelialize.<sup>34</sup> The donor site should be drained with a Penrose or TLS drain.

A vesicovaginal fistula occurring in an irradiated field is at significant risk for compromised healing, and consideration should be given for a biopsy to rule out persistent malignancy in the appropriate patient. The bladder capacity and compliance

should be determined prior to surgery in case augmentation is required. Interpositional grafts should always be considered in irradiated patients, as



**Figure 23.13** The bladder is closed in two layers—the mucosal layer first, followed by the muscle layer. An SP tube should be placed before final closure. An interpositional graft such as peritoneum or omentum can be placed between the two completed closures.

the first procedure is always the best procedure. Most success rates in previously reported series involving irradiated tissues are about 50%.<sup>35</sup>

#### *Postoperative care*

Patient management after any approach is similar. Uninterrupted urinary drainage with both suprapubic and urethral catheters is indicated. Bladder spasms should be controlled with oral or intrarectal anticholinergics, as high intravesical pressure must be avoided. Perioperative full-dose and postoperative low-dose antibiotics should be considered for as long as the catheters are in place. The use of estrogen cream postoperatively may promote vaginal healing and should be considered, especially in elderly women. In addition, vaginal manipulation and intercourse should be avoided for 4–6 weeks postoperatively to avoid suture line tension.

Catheter drainage should be carried out for at least 14 days postoperatively and is followed by a VCUG (off all anticholinergics) to ensure fistula tract closure. With confirmation of fistula tract closure, the urethral catheter is removed. After the patient demonstrates adequate voiding capabilities, the suprapubic catheter may be removed.

#### *Complications*

Complications pertinent to the surgery include fistula recurrence, injury to surrounding structures, and dyspareunia. Recurrent fistulas identified immediately should be managed

conservatively. Persistent, recurrent fistulas should be repaired after vaginal mucosal inflammation subsides. Secondary repair may be successful in a majority of cases but usually requires transabdominal surgery. A laparoscopic approach may be suitable in the appropriate individual but requires advanced laparoscopic skills. Endoscopic and percutaneous approaches can usually be used to manage ureteral obstruction if it should occur after surgery. In many cases, the obstruction is secondary to edema and will subside with a few weeks of stenting. Finally, vaginal stenosis, while rare, may be successfully managed with relaxing incisions and vaginal interpositional grafts to increase the vaginal dimensions.

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## Laparoscopic treatment of benign testicular disorders and hernias

James F Donovan, Adam R Metwalli, and Marcy J Abel

### Varicoceles

Varicoceles are a common condition present in approximately 15% of adult males.<sup>1</sup> As in other areas of urology, minimally invasive alternatives to traditional open procedures have become popular for varicocele ligation. Laparoscopic varix ligation was first described in 1988 and has since evolved with new instrumentation and techniques.<sup>2</sup> Whether laparoscopic methods offer an advantage over traditional open procedures remains controversial.<sup>3,4</sup>

#### *Diagnosis, work-up, and staging*

Typically presenting in adolescence, varix represents a dilation of the pampiniform plexus of spermatic veins. Varicoceles are most often identified on the left side (80–90%) but may be bilateral in 50% of patients; rightside-only varicoceles are unusual and prompt further diagnostic evaluation to rule out proximal venous obstruction due to mass. The development of a varicocele is attributed to increased pressure within the renal vein due to the compression of the renal vein by the superior mesenteric vein and/or the acute angle of anastomosis between the gonadal vein and the renal vein on the left and/or the incompetence or absence of venous valves.

Collateral venous channels often contribute to varix formation. While the majority of men with varicocele are asymptomatic, varices are clinically significant when associated with testicular pain or male subfertility. Forty percent of those with primary infertility and 80% of those with secondary infertility are related to varicocele formation and remain the most common indication for repair.<sup>5</sup>

Varicoceles are graded based on physical examination, with large varicoceles visible on inspection (grade III), medium varicoceles palpable without Valsalva maneuver (grade II), and small varicoceles only palpable during Valsalva's maneuver (grade I). Careful physical examination is essential and must be performed in a warm room with the patient standing. The examiner supports the testicle and thereby shortens the spermatic cord to eliminate the sense of filling in anticipation of the cremasteric muscle contraction during Valsalva's maneuver. Sometimes mistaken for varicoceles, cord lipomas can be distinguished by pinching the cord fullness; unlike a varicocele, which compresses between the examiner's fingers, a lipoma will slip from grasp.

Color Doppler ultrasonography may confirm the presence of a varicocele when the physical examination is equivocal or identify a contralateral varicocele prior to repair.

Other radiologic modalities, including contact thermography, radionuclide angiography, and percutaneous spermatic venography (PSV), have also been used to diagnose varices. The use of sophisticated imaging modalities to identify subclinical varices is controversial. Despite reports of improved fertility with repair of the subclinical varix, invasive testing, lack of equipment, and high rate of false-positive results have limited the use of advanced radiologic modalities. We do not search for or repair subclinical varicoceles.

### *Indications and treatment options*

Indications for varicocele treatment in the adult include (1) scrotal pain without other identifiable intrascrotal abnormalities or (2) male subfertility in the presence of an abnormal seminal fluid analysis and a partner free of female factors contributing to infertility. The most common indication in adolescence is testicular growth retardation, which is evident when the ipsilateral testicular volume is significantly less than that of the contralateral testes. Evaluation and treatment for the adolescent varicocele is addressed elsewhere in this chapter.

The ideal method of varicocele repair remains controversial. Both operative and nonoperative treatment options are available. Nonoperative therapy consists of transvenous ablation of dilated spermatic vessels, typically performed by an interventional radiologist. Open surgical procedures include approaches at the retroperitoneal (Paloma—highest), inguinal ((Ivanissovitch—middle), or subinguinal (Marmar-Goldstein—lowest) level. Lap- aroscopic varix ligation was described using a single transabdominal trocar in 1988 by Sanchez de Badajoz.<sup>2,6</sup> In this method spermatic vessels are transected just proximal to the internal ring via a transperitoneal approach. Excellent visualization of the spermatic vessels and collaterals traversing the internal ring is attained. Although large prospective randomized trials are lacking, multiple series report equal efficacy of the laparoscopic technique to traditional open procedures when comparing varicocele recurrence, improvements in semen analysis, and overall pregnancy rates.<sup>7–13</sup>

The number of venous tributaries varies with each approach: more tributaries are present at lower levels, fewer tributaries are evident at higher levels. In addition to the increase in numbers of veins, the distal spermatic cord contains the confluence of testicular artery collateral branches, including testicular artery, cremasteric artery, and artery to the vas deferens. Thus, with inguinal and subinguinal approaches, care must be taken to avoid compromise of the testicular artery and collaterals. Concerns for compromise of testicular blood supply and potential deleterious effects on sperm quality postoperatively prompted testicular artery preservation. Recently, reports comparing testicular blood flow and pregnancy rates following laparoscopic varix ligation have found no significant difference between testicular artery sparing and testicular artery ligation.<sup>1,14–17</sup> Moreover, Kattan found increased incidence of varicocele recurrence after arterial preservation, presumably due to increasing caliber of small, undivided, residual venules intimately adherent to the testicular artery.<sup>18</sup> We no longer preserve the spermatic artery.

### *Patient selection and contraindications*

Strict attention to minimizing complications has guided patient selection for laparoscopic repair. Concerns for abdominal wall adhesions and subsequent bowel injury during placement of the Veress needle made previous abdominal surgery a relative contraindication for laparoscopy. We use an open laparoscopic technique with Hasson cannula in patients who have a history of prior laparotomy or peritonitis. Other considerations include obesity, which remains a relative contraindication as trocar placement and instrument manipulation may be difficult. An absolute contraindication to laparoscopic varix ligation is a history of prior Paloma repair; patients who have undergone previous Paloma repair are likely to not benefit from laparoscopic varix ligation wherein vessels are transected at the similar retroperitoneal level.

### *Patient and preoperative preparation*

In addition to the risks and benefits of varix repair, complications unique to laparoscopic repair should be discussed with the patient, including possible conversion to open surgery to repair intestinal injury or vascular injury.

All procedures are performed as outpatients. Bowel preparation is not performed routinely. General anesthesia is necessary because pneumoperitoneum with CO<sub>2</sub> is not tolerable. Skin preparation includes the abdomen and genitals. The stomach is decompressed with a nasogastric tube and the bladder emptied with straight catheter. The skin is draped to allow access to the lower abdomen and genitals—traction on the testes will help in identification of the spermatic vessels above the internal ring.

### *Recommended equipment and instruments*

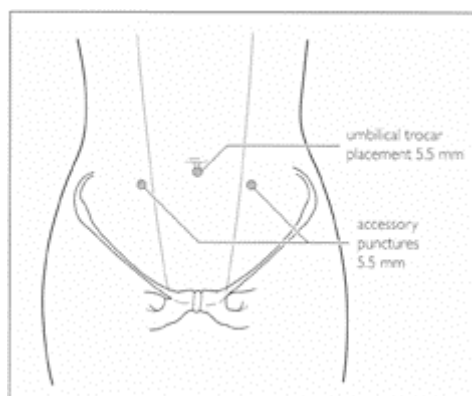
We obtain peritoneal access with the Veress needle or selective use of the Hasson cannula. In most cases, three 5 mm trocars are used with a 5 mm 45° laparoscope. Dissection utilizes a curved scissors with electrocautery and a curved dissector. A 5 mm hemoclip applier is used during venous ligation. If venous bundles are too large to be clipped with a 5 mm hemoclip, we tie with 2–0 silk ligature using an intracorporeal tying technique. Equipment and instrument requirements are summarized later in Table 24.2.

### *Procedure: laparoscopic varix ligation*

We make an 0.5 cm vertical sub umbilical incision and insert a Veress needle into the peritoneal cavity. Following appropriate tests to assure intraperitoneal Veress position, insufflation proceeds to a pressure of 20 mmHg. The Veress needle is removed and a 5 mm trocar is inserted through the subumbilical incision. We then place the patient in Trendelenburg's position to mobilize the peritoneal viscera cephalad. The 5 mm 45° laparoscope is inserted and inspection assures no injury due to Veress needle or trocar insertion.

Two additional 5 mm ports are placed under direct vision (Figure 24.1). The optimal position for each port is lateral to the rectus muscle and just below the level of the

umbilicus. If the varix ligation is unilateral, then an alternate port position would be through the midline midway between the umbilicus and the pubic symphysis in place of the port lateral to the contralateral rectus muscle.

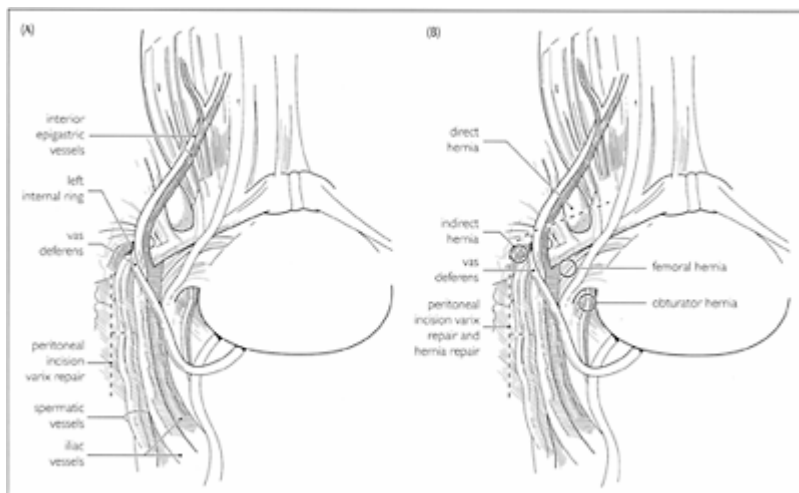


**Figure 24.1** Position of laparoscopic trocars for unilateral or bilateral varix ligation: midline subumbilical and bilateral paramedian just below the umbilicus. All trocars are 5 mm and the 45° laparoscope may be placed in either the subumbilical or the ipsilateral port.

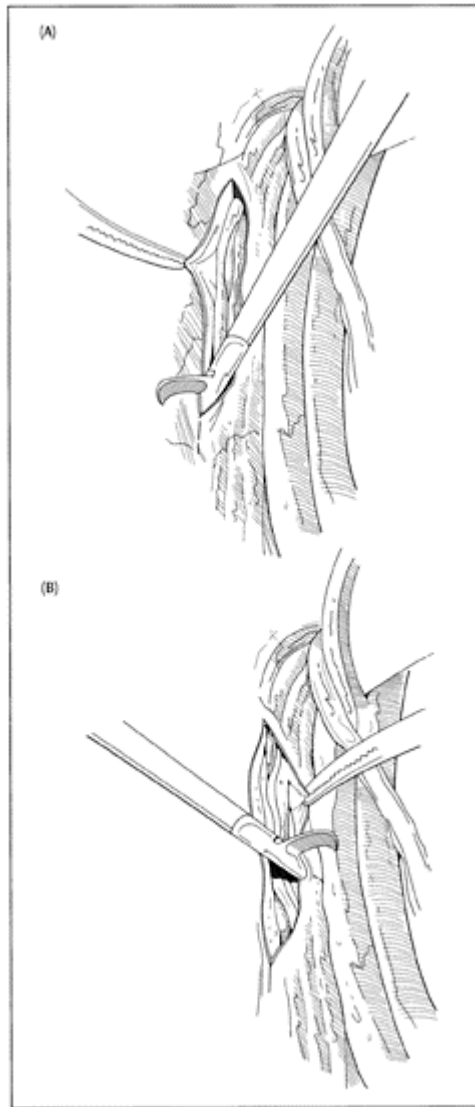
We turn our attention to the varix ligation. To expose the spermatic vessels, sigmoid colon or overlying bowel is mobilized if necessary. A 3–5 cm incision is made parallel and lateral to the spermatic vascular bundle 3 cm above the internal ring (Figures 24.2A, 24.3A). The medial flap of the peritoneum is grasped and the underlying vessels are swept away bluntly. A perpendicular ‘T’ incision is made at the midpoint of this incision and carried to the lateral aspect of the iliac artery, exposing the vascular bundle (Figure 24.3B).

The vascular bundle is then cleared of overlying adventitial tissue and dissected free from the underlying psoas muscle (Figure 24.4). Typically, 3–8 spermatic veins are identified and can be separated into smaller bundles in anticipation of clip ligation and transection. The artery is usually single and located posterior and medial to the venous bundle. If arterial preservation is contemplated, then careful dissection will expose the artery and separate the veins. The 5 mm hemoclip is used to clip-ligate veins which are not too large (Figure 24.5A). If the 5 mm clip is not able to provide safe occlusion, then a piece of 2–0 silk is passed into the peritoneal cavity and passed around the



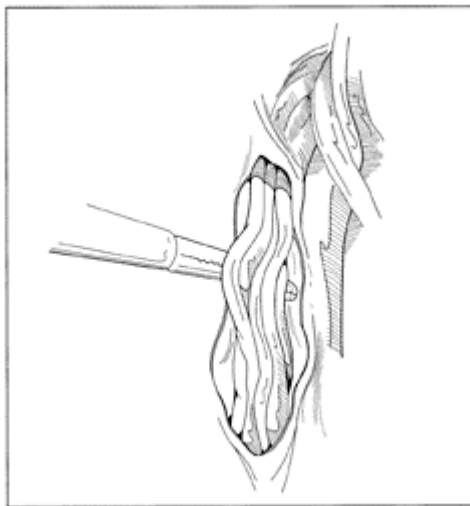


**Figure 24.2** (A) The left spermatic veins and neighboring anatomy. A ‘T’ incision is made with incision parallel and lateral to the spermatic veins. (B) Retroperitoneal anatomy related to inguinal hernias. Sites for direct, indirect, femoral, and obturator hernias are shown. Inverted V incision can be used for combined varix ligation and trans-abdominal preperitoneal hernias. When hernia repair alone is planned, the lateral incision can be made over the external iliac artery. The transverse incision above the internal ring extends to the obliterated umbilical artery medially and just beyond the internal ring laterally.



**Figure 24.3** (A) Incision through peritoneal membrane lateral and parallel to the spermatic vessels. (B) 'T' incision from midpoint of lateral incision extends medially up to the external iliac artery. The undersurface of the peritoneum is cleared first, then

the membrane divided to expose the underlying spermatic vessels.



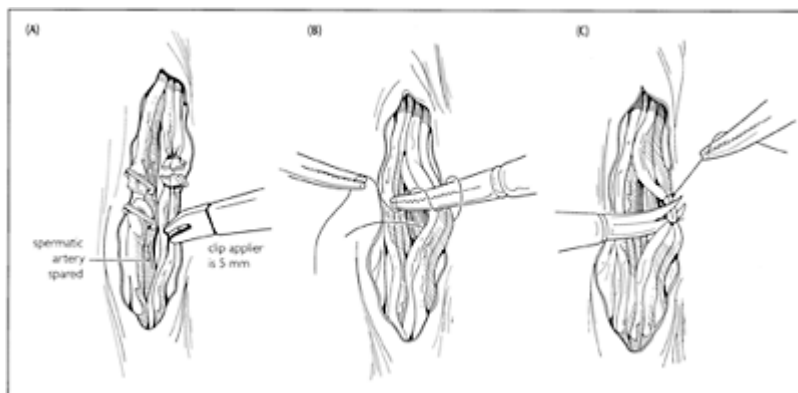
**Figure 24.4** The entire spermatic vascular bundle is mobilized using sharp and blunt dissection. Care is taken to avoid deep dissection thus protecting the underlying genitofemoral nerve.

venous bundle, and then tied using either intracorporeal or extracorporeal knot-tying techniques (Figure 24.5B).

Upon completion, we perform a systematic exit from the abdomen. Intraperitoneal pressure is reduced to 8 mmHg and the operative site is inspected for hemostasis. Small bleeding is best stopped by judicious use of electrocautery. The patient is taken out of Trendelenburg's position and irrigant and blood are aspirated from the pelvis. Trocars are removed under direct vision while maintaining 5 mmHg pressure. Each insertion site is examined for bleeding following trocar removal. The overlying skin is then closed with subcuticular suture or with Dermabond (Ethicon, Inc. Division of Johnson & Johnson).<sup>1</sup> We perform formal fascial closure only if we have used a >10 mm trocar.

### *Results*

An initial series of laparoscopic varix ligation reported low recurrence rates of 1.0–1.6%<sup>19,20</sup> and pregnancy rates of 26–46%,<sup>8,21</sup> which were similar to those reported following traditional open ligation.<sup>22,23</sup> Others have compared laparoscopic varix ligation to open varicocelectomy and



**Figure 24.5** (A) Sharp and blunt dissection divides the spermatic vessels into bundles sufficiently small to permit laparoscopic varix ligation with hemoclips. (B) An alternative to hemoclips is ligation with 2–0 silk tied intracorporeally. (C) Spermatic vascular bundles are divided sequentially—exposing any underlying veins—until none remain. Sparing the testicular artery does not offer any advantage but may be considered in patients who have undergone inguinal surgery which might compromise the integrity of collateral circulation.

sclerotherapy: there was no significant difference in varix recurrence, pregnancy rates, or measured improvement in seminal fluid analysis.<sup>9,12,13</sup>

Laparoscopic varix ligation has shown equally good outcomes in those patients being treated for painful varicoceles with 84% resolution.<sup>24</sup> Brooks and associates treated a male who had undergone varix ablation with embolization using Gianturco coils but who had developed increasing pain, which ultimately responded to laparoscopic varix ligation, including the testicular artery.<sup>25</sup> Subsequently, Cadeddu et al reported a series of testicular cord denervations performed on patients with intractable orchalgia.<sup>26</sup> Of nine patients included in the study, 8 had undergone prior scrotal surgery and all had failed nonoperative treatments. Seven (77%) patients demonstrated significant response (the mean analog pain score was reduced from 69 to 19).

Complications following laparoscopic varix ligation are few: 1.3% in a series of 766 procedures.<sup>27</sup> Wound infection, hydrocele, hematoma, epididymitis, and pain are the most frequently reported complications. The complications rate appears to be declining in

recent years, and in recent series complications have occurred less frequently in those undergoing laparoscopic repair compared with other methods.<sup>12,24</sup> However, Sautter and associates report hydrocele (17%), epididymitis (7%), and prolonged pain (12%) following laparoscopic varix ligation.<sup>9</sup> Major complications from laparoscopic varicocele ligation such as vascular injury, loss of testicle, or intestinal injury are rare and reported at 0–4%.<sup>7,8,28,29</sup> In most series, laparoscopic ligation was performed on an outpatient basis with few exceptions, comparable to our experience.

### *Conclusions*

With sufficient training and experience, the laparoscopic method of repair offers a safe and effective alternative to previous methods of varicocele ligation. With a relatively short learning curve, this method can be integrated into the armamentarium of varicocele treatment options in most urology practices. The most obvious advantage of laparoscopy would be decreased morbidity and quick recovery time. Further randomized trials are needed to clearly elucidate the possible benefit of laparoscopy over traditional open procedures.

## **Inguinal hernia**

Inguinal hernias are categorized as direct, indirect, femoral, or obturator, based upon the location and character of the anatomic defect. Indirect hernias are most common and involve projection of the peritoneal membrane in continuity with persistent process tunica vaginalis through the internal ring and into the inguinal canal. Direct hernias describe an acquired protrusion of the peritoneal membrane through Hasselbach's triangle. Femoral and obturator hernias occur through the femoral and obturator canals, respectively (Figure 24.2B).

### *Diagnosis, work-up and staging*

Typically, patients with inguinal hernia present with a mass and/or pain in the groin. Both mass and pain (usually described as sharp) may vary with body position or level of exertion. The physical examination includes inspection of the inguinal area to detect asymmetry, followed by digital palpation through the external ring to detect protrusion either through the internal ring or through the floor of the inguinal canal (Hasselbach's triangle) during Valsalva's maneuver. Bilateral examination is essential, since 10–25% of patients undergoing laparoscopic repair of unilateral inguinal hernias are found to have contralateral pathology.<sup>30–32</sup> The addition of computer tomography (CT) or magnetic resonance imaging (MRI) may be helpful in equivocal cases.

### *Indications and contraindications for laparoscopic repair*

Infection is an absolute contraindication for hernia repair with synthetic mesh, irrespective of the surgical approach. A relative contraindication for any transabdominal laparoscopic procedure is multiple previous abdominal explorations with known

adhesions. Severe cardiopulmonary disease is a relative contraindication for laparoscopic herniorrhaphy since it requires general anesthesia. Inability to reduce the hernia in an anesthetized patient is a contraindication for the laparoscopic extraperitoneal approach.<sup>33</sup>

Increased cost has also been mentioned as a relative contraindication for laparoscopic herniorrhaphy.<sup>34</sup> However, given the shortened recovery period after laparoscopic herniorrhaphy and the decreased requirement for analgesia postoperatively, it is likely that longer-term cost analyses will prove that the initial increase in short-term expense is more than overcome by cost savings in the form of fewer lost working days.<sup>35</sup>

### *Treatment options*

Laparoscopic inguinal hernia repairs are divided into three categories:

1. intraperitoneal or intraperitoneal-onlay mesh (IPOM)
2. transperitoneal or transabdominal preperitoneal (TAP) technique
3. totally extraperitoneal (TEP) approach.

The IPOM procedure entails suturing or stapling synthetic mesh over the internal ring and Hasselbach's triangle through the peritoneal membrane. Because the preperitoneal fascial landmarks are not exposed, the reliability of this approach is suspect due to one's inability to assure secure fixation of the mesh to the underlying fascial structures. Fixation to the peritoneum alone will result in migration of the peritoneal surface and mesh into the fascial defect, leading to recurrence. We do not endorse this approach.

The TAP operation traverses the peritoneum, but elevation of a peritoneal membrane flap provides exposure to the preperitoneal space where the mesh is secured to the transversalis fascia and Cooper's ligament to cover the internal ring and Hasselbach's triangle; the peritoneal flap then covers the synthetic mesh, thereby preventing contact between mesh and intestine. The TEP approach creates working space in the preperitoneal space with balloon or fluid or gas followed by reduction of direct or indirect hernia and fixation of mesh over Hasselbach's triangle and the internal ring.

### *Patient and preoperative preparation*

Preoperative evaluation is dictated by standard of care and patient's comorbidities. Bowel preparation is left to the surgeon's discretion. All laparoscopic herniorrhaphies utilize synthetic mesh, which mandates the administration of antibiotic prophylaxis. Contraindications to laparoscopic hernia repair are listed in Table 24.1.

### *Equipment*

An excellent surgical repair begins with ensuring that the proper instruments are readily available to the surgeon prior to the start of the case. A list of necessary equipment is provided in Table 24.2. For all pelvic laparoscopic operations, the video monitor is positioned at the foot of the table. The right-hand dominant surgeon will stand at the patient's left side. The patient's arms are padded and tucked at the sides to avoid brachial plexus stretch when the surgeon or the assistant move cephalad during the operation.

In the TAP approach, at least one 10 mm trocar is needed for the laparoscope and mesh insertion. Operating

### **Table 24.1** *Contraindications to laparoscopic hernia repair*

#### Absolute

Infection (all approaches—use of synthetic mesh is prohibited)

History of pelvic radiation

Prior preperitoneal surgery (TAP and TEP—i.e. prostatectomy)

#### Relative

COPD (all approaches—increased intraperitoneal

Anticoagulation pressures and CO<sub>2</sub> absorption)

Multiple abdominal procedures (i.e. TAP—adhesions may prevent exposure)

Irreducible hernia (i.e. TEP—contents must be inspected transabdominally)

Suspected contralateral hernia (i.e. TEP—contralateral hernia best confirmed transabdominally)

COPD, chronic obstructive pulmonary disease; TAP, transabdominal preperitoneal technique; TEP, totally extraperitoneal technique.

trocars may be either 5 mm or 10 mm: a 10 mm trocar is necessary if using a 10 mm hernia stapling device, whereas a 5 mm trocar can accommodate the mesh-tacking device. Some laparoscopic surgeons prefer a blunt Hasson-type trocar for the initial trocar placement at the umbilicus.

The TEP approach requires development of a preperitoneal working space. A balloon device is available for initial dissection in the space of Retzius followed by insertion of a 10 mm balloon retention trocar which provides access for the laparoscope and mesh insertion. Alternatively, Wolf and Soper adapted Gaur's technique using a surgical glove finger secured over a red-rubber catheter, which offers an inexpensive alternative.<sup>36,37</sup> Instrument trocars are either 5 mm or 10 mm. We have used 5 mm trocars with the fascial tacking device.

### *Surgical techniques*

#### **Transabdominal preperitoneal approach**

Following insufflation through a Veress needle, the surgeon inserts a 10 mm trocar below the umbilicus and inspects the peritoneal cavity—the presence of bilateral hernias will influence the size and location of additional trocars.

Typically, two additional ports are placed just below the umbilicus lateral to the rectus muscles; one 10 mm trocar placed on the contralateral side and one 5 mm trocar placed on the ipsilateral side. The larger trocar is intended to accommodate a hernia stapling device—if a tacking device is used, then both added ports may be 5 mm. Taking care to avoid the deep inferior epigastric vessels, we use

**Table 24.2** *Equipment requirements for laparoscopic varix ligation and laparoscopic inguinal and ventral hernia repair*

|  | Varix ligation | Inguinal hernia | Ventral/incisional hernia |
|--|----------------|-----------------|---------------------------|
| 5 mm laparoscope (30° or 45°)                        | +              | —               | —                         |
| 10 mm laparoscope (0° and either 30° or 45°)         | —              | +               | +                         |
| 10 mm trocar   | —              | 1 or 2*         | 1 or 2*                   |
| 5 mm trocar  | 3              | 1 or 2*         | 1 or 2*                   |
| Scissors   | +              | +               | +                         |
| Dissector  | +              | +               | +                         |
| PDB balloon and PDB blunt tip trocar <sup>a</sup>    | —              | TAP–/ TEP+      | —                         |
| Hemoclip device                                      | +              | —               | —                         |
| Hernia stapler (mandatory for TAP)                   | —              | +               | —                         |
| Mesh fixation device: hernia stapler or helical tack | —              | +               | +                         |
| Mesh   | —              | +(Nonspecific)  | +(DualMesh)               |
| Suction-irrigation                                   | Optional       | Advised         | Advised                   |

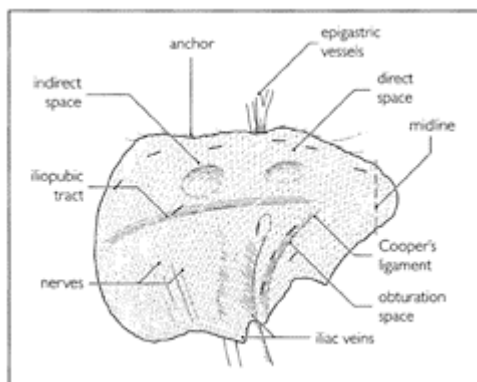
TAP, transabdominal preperitoneal technique; TEP, totally extraperitoneal technique. <sup>a</sup> PDB balloon and blunt tip trocar by US Surgical, Norwalk, Connecticut.

scissors to incise the peritoneal membrane 4 or 5 cm anterior to the hernia defect and extending from the medial umbilical peritoneal fold to a position several centimeters past the internal ring (Figure 24.2B). Cautery should not be applied lateral to the epigastric vessels in order to avoid nerve damage. Sharp and blunt dissection retracts the peritoneal membrane medially to expose Cooper's ligament, the inferomedial limit of dissection.

The peritoneum overlying the cord structures should be grasped and retracted posteromedially, exposing the lateral iliopubic tract. Transection of the hernia sac should be performed if reduction of the sac cannot be performed safely or if the sac is very large. The peritoneal membrane should be retracted posteromedially using a 'hand over hand' technique with graspers until the sac is completely everted into the midpelvis, freeing the cord structures which lie deep. If necessary, division of the hernia sac should be performed carefully about 2–3 cm distal to original neck of the sac and the proximal peritoneotomy can be closed with a pre-tied loop. Sufficient peritoneal membrane must be preserved to enable closure over the mesh repair.

Following exposure of the iliopubic tract and Cooper's ligament, we insert the prosthetic mesh. To reduce the chance of recurrence, one must use a piece of mesh large enough to cover both direct and indirect defects with no less than 2 cm overlap of mesh beyond the anatomic borders of Hasselbach's triangle and internal inguinal ring (Figure 24.6). The minimum dimensions for mesh repair are 5 cm×10 cm, but most authors recommend a much larger prosthesis.<sup>37–39</sup>

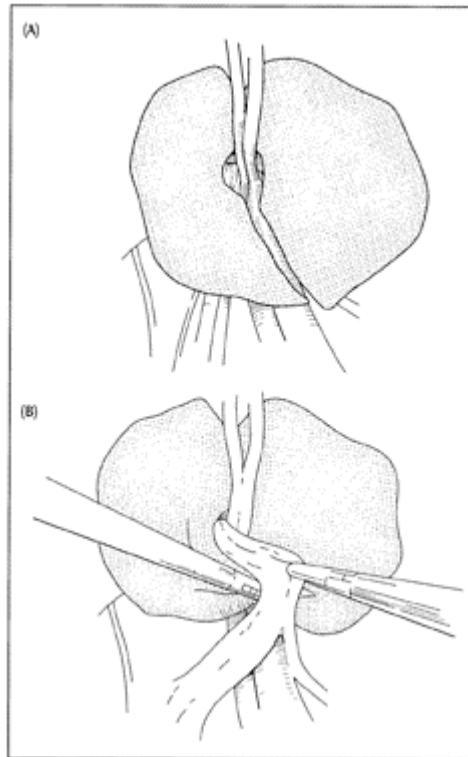




**Figure 24.6** Appropriate mesh placement should cover other potential hernia sites such as direct, inguinal, and femoral canals. Staples or tacks should not be placed cephalad or lateral to the internal ring over the psoas muscle to avoid risk of nerve injury. Note: staples in Cooper's ligament.

While the merits of incising the mesh vertically to create a defect to accommodate the spermatic cord and/or the inferior epigastric vessels (Figure 24.7) are debated, laparoscopic surgeons agree that the peritoneal membrane must be dissected cephalad to assure that the inferior edge of mesh is deep to the leading edge of peritoneum—failure to do so promotes recurrence with intraperitoneal pressure on the peritoneum advancing underneath the mesh and into the inguinal defect.

Introducing the mesh into the abdominal cavity is a matter of surgeon preference as there are a myriad of methods. Most involve rolling the mesh in order to pass it through a 10 mm trocar. Some surgeons suggest that passing the rolled mesh through the trocar using a 5 mm grasper is all that is necessary.<sup>39</sup> Others find that



**Figure 24.7** (A) and (B) Some laparoscopic surgeons prefer to split the mesh and place it around the spermatic cord and between the deep inferior epigastric vessels and the rectus muscle, which requires careful dissection of vessels from underlying muscles. Measurable benefit of this time-consuming technique is not substantiated.

backloading the mesh into a reducer sleeve or a 26F Amplatz sheath or an appendiceal extractor facilitates inserting the mesh into the operating field.<sup>37-39</sup>

Once the mesh is unrolled within the peritoneal cavity, proper placement of the prosthesis requires positioning over the defect(s) so that sufficient overlap allows coverage of potential herniation sites and mesh fixation to healthy tissue (see Figure 24.6). Placement of the stapler through the contralateral trocar makes fixation somewhat easier, as does the bimanual technique of stapling. This method uses the hand not holding the stapler to exert pressure on the ipsilateral abdomen or groin so that the tip of the

stapler is palpable through the abdominal wall. Parallel orientation of the staples to the regional nerves can also minimize nerve entrapment.<sup>39</sup> The medial landmark for fixation is the pubic symphysis, where several staples can be placed easily without concern for injury to adjacent structures. Cooper's ligament, the inferomedial site of mesh fixation, will accommodate 4–6 staples and is vitally important to ensure adequate fixation of the mesh. Superiorly, the mesh is tacked to the transversalis fascia. No staples should ever be placed below the iliopubic tract lateral to the internal spermatic vessels, avoiding injury to the lateral femoral cutaneous nerve and the femoral branch of the genitofemoral nerve.

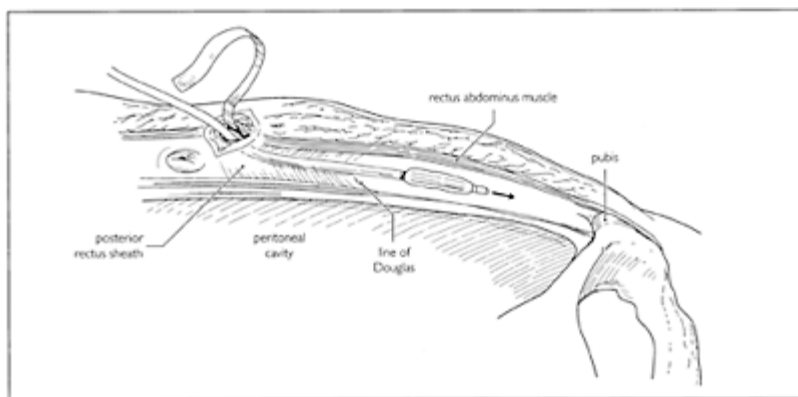
To close the peritoneum over the prosthesis, we reduce the pneumoperitoneum pressure. This confirms proper position of the mesh, permits inspection for bleeding, and reduces tension to facilitate closure of the peritoneal membrane eliminating gaps which might result in recurrent hernia or bowel obstruction. Next, large (>10 mm) port sites are closed with fascial sutures (2–0 absorbable monofilament) using a suture passing device. Trocars are removed under direct vision with low-pressure pneumoperitoneum. All wounds are closed with interrupted 3–0 absorbable subcutaneous and subcuticular sutures.

### **Totally extraperitoneal approach**

With the patient in the supine position and under sterile conditions, we make a subumbilical incision which enters the rectus abdominis anterior sheath just off midline to the side of the hernia (or to the side of the larger hernia in cases of bilateral hernia), avoiding the linea alba and urachus.<sup>40</sup> Incision of the anterior rectus sheath is followed by retraction of the rectus muscle laterally using S-retractors, exposing the posterior rectus sheath. Blunt finger dissection of the space between the rectus muscle and the posterior rectus sheath is carried down to the pubis.

Next, development and insufflation of the preperitoneal space begins. One may choose dissection, clearing a space between the peritoneum and the pubis. Alternatively, one may insert a subumbilical trocar and proceed with insufflation followed by addition of instrument trocars to allow the dissection of the preperitoneal space.

Balloon dissection (either commercially available or surgical glove with red rubber catheter) offers blunt dissection with minimal trauma and tamponade of small bleeders. The balloon dissector should be advanced to the pubic symphysis through the space of Retzius (Figure 24.8).

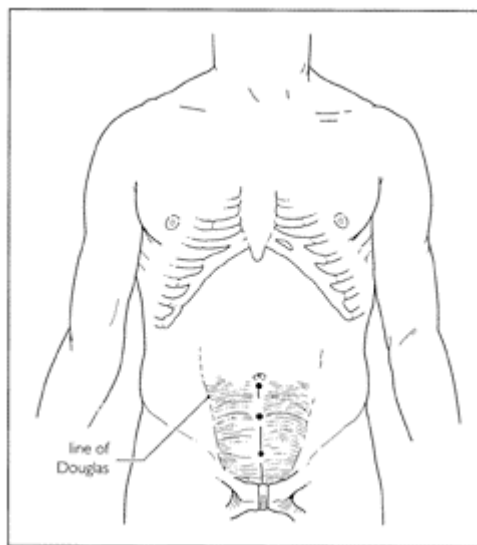


**Figure 24.8** Development of extraperitoneal space with balloon dissector creating working area between rectus muscle and posterior rectus sheath down to pubis.

Once the balloon dissector assembly is advanced to the pubis, inflation can proceed. This requires room air (in the case of commercial balloons) or water (in the case of glove-catheter device) inflation.<sup>37,40</sup> If bowel or intraperitoneal contents are identified at any point during development of the preperitoneal space, insufflation should stop and the operation converted to TAP or open repair. One advantage of balloon dilation compared to gas insufflation only is that strands of connective tissue between the peritoneum and the body wall are more completely disrupted with the balloon.<sup>37</sup>

Once the extraperitoneal space has been developed, we insert a blunt 10 mm trocar deep to the posterior rectus fascia and insufflate to 12 mmHg. Additional trocars are placed below the peritoneal reflection created by balloon dissection. Some authors recommend all trocars be placed in the midline (subumbilical, suprapubic, and midway between) (Figure 24.9). Others prefer to place the midway trocar in a lateral position, just medial to the iliac crest on the side ipsilateral to the hernia.<sup>37,40</sup> Trocar placement should be performed under direct vision to avoid puncture of the peritoneal membrane or laceration of the inferior epigastric vessels.

After inspection of the preperitoneal space and division of any remaining connective tissue strands between the abdominal wall and the peritoneum, we identify Cooper's ligament, carefully exposing the pubic ramus from midline to the external iliac vein laterally.



**Figure 24.9** Midline trocar placement for TEP repair

Direct hernia and small indirect hernia sacs are reduced with blunt dissection. Occasionally, the direct hernia requires incision of the fascia at the superior-anterior edge to reduce an incarcerated sac. Caution must be exercised to avoid injury to the bladder, which may adhere to the medial sac.

Inspection of the femoral canal, lateral to Cooper's ligament and medial to the femoral vein, determines the presence or absence of femoral hernia. If present, a femoral hernia must be reduced with blunt and/or sharp dissection. Once the direct and femoral components have been addressed, the spermatic cord is examined for the presence of a cord lipoma which may interfere with proper placement of prosthetic mesh. If present, the lipoma should be retracted out of the internal ring and either excised or placed in the retroperitoneum away from the operative field. The femoral branch of the genitofemoral nerve and the lateral femoral cutaneous nerve are often found directly beneath cord lipomas—gentle dissection without cautery is imperative.

Dissection of the peritoneum away from the vas deferens and as far cephalad as possible allows the mesh to be covered by peritoneum after release of insufflation; it also prevents lifting of the medial aspect of the mesh. If present, an indirect hernia sac will be found anterolateral to the cord structures. Small hernias should be easily retracted out of the internal ring, whereas larger sacs may require 'hand-over-hand' retraction with atraumatic graspers in order to reduce the hernia. Complete dissection of the sac and its attachments into the retroperitoneum well above the site for the prosthesis is necessary to prevent recurrence. As with the transabdominal technique, long, narrow hernia sacs or extremely scarred and adherent sacs are better transected near the internal ring rather than risk injury to the cord structures during a difficult dissection. The proximal peritoneotomy can be closed with an Endoloop or ligature.

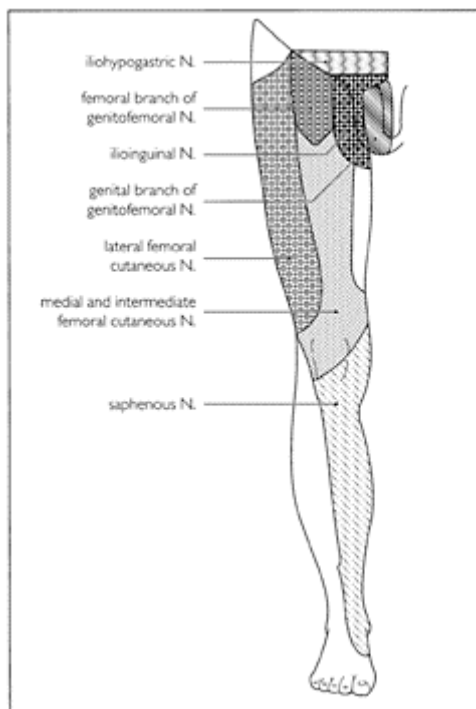
Placement of mesh is similar to the TAP procedure. The mesh must be large enough to cover all three potential hernia locations with adequate overlap (see Figure 24.6). Placement of the mesh on top of or around the spermatic cord is according to surgeon preference. Fixation of the prosthesis, removal of instruments, and closure of incisions follow the same rules described for the transabdominal repair.

### *Complications*

The overall complication rate for laparoscopic herniorrhaphy has been reported as between 5–16%.<sup>41–45</sup> Infection of the mesh is a rare occurrence with rates less than 1%.<sup>41</sup> The incidence of minor complications seems to be comparable between laparoscopic and open techniques, but laparoscopy appears to have more vascular and visceral injuries.<sup>46</sup>

In laparoscopic herniorrhaphy, the use of a ‘plug’ in addition to the patch repair is contraindicated because the mesh plug tends to migrate into the scrotum or labia, requiring additional surgery. The recurrence rate for this has been reported as between 9 and 22%, which is more than five times the recurrence rates for other laparoscopic techniques.<sup>41,42</sup>

Nerve entrapment is perhaps the most troublesome complication of all hernia surgeries. As boundaries for laparoscopic mesh fixation have been established, the incidence of postoperative neuralgia has decreased significantly<sup>47</sup> (Figure 24.10). Meta-analyses of studies comparing laparoscopic herniorrhaphy to open repair have revealed a lower incidence of chronic numbness in patients treated laparoscopically.<sup>46</sup> The rates for neurologic complications typically range from 1–2% but have been reported as high as 4.6%.<sup>42,48</sup> Treatment of postoperative neuralgia consists of nonsteroidal anti-inflammatory drugs (NSAIDs) and observation, with resolution of symptoms over 2–4 weeks.



**Figure 24.10** Distribution of sensory nerves of the leg and common sites for postoperative neuralgia.

in most patients. Occasionally, persistent pain requires a procedure to remove the staple causing symptoms.

Fixation of the prosthesis to the pubic or pelvic bones may result in osteitis. This condition is treated in a similar manner as neuralgia. If fibrin glue fixation eventually proves to be as effective and economical as staples or tacks, this complication may be eliminated.

Testicular and scrotal pain may occur after laparoscopic herniorrhaphy and is often associated with complete dissection of the hernia sac away from the cord. This can be avoided by only partially dissecting large sacs that extend into the scrotum. Scrotal hematomas, hydroceles, and lymphoceles are also more common after complete excision of the hernia sac. With secure fixation of the mesh over the direct and indirect defects, complete dissection of the hernia sac is unwarranted. Most cases of orchitis and orchalgia will resolve spontaneously once alternate venous and lymphatic drainage patterns have developed.

Small bowel obstruction has been reported as a complication of the TAP and IPOM herniorrhaphy, but has only been reported once after a TEP repair.<sup>40</sup> Obstruction occurs as a result of poor peritoneal closure and may also be due to herniation through trocar sites. Omentum tends to herniate through port sites more often than bowel. Closure of

trocar sites larger than 5 mm significantly reduces the risk of port-site herniation and subsequent bowel obstruction.

Complications specific to the TEP technique are generally associated with development of the preperitoneal space. Avulsion of the inferior epigastric vessels or other accessory vasculature can cause significant bleeding. This complication is more common with balloon dissectors that extend laterally. If the development of the preperitoneal space results in separation of the inferior epigastric vessels from the abdominal wall, ligation or cautery of these vessels is important, as they will be at risk for injury during further dissection.

### *Results*

Ongoing modifications in technique and advances in laparoscopic equipment continue to improve the results of laparoscopic procedures. The decreasing incidence of post-operative neuralgia is largely due to avoidance of stapling below the iliopectic tract, and port-site herniations are increasingly rare as more instruments that operate through 5 mm trocars become available and the practice of closing 10 mm and larger trocar defects has become standard. The short- and long-term recurrence rates for TAP and TEP repairs are comparable to those of open herniorrhaphy. The EU Hernia Trialists Collaboration analyzed the data from 34 reports, including 6804 randomized patients, and found that the recurrence rate for laparoscopic repairs was 2.3% compared with 2.9% for open herniorrhaphy.<sup>46</sup> These rates of recurrence are consistent with other reports in the literature; there appears to be little difference between TAP and TEP, but IPOM with or without 'suffer higher recurrence rates'.<sup>41,42,44,45,49-53</sup>

Operating time is usually longer for laparoscopic repair: operating times for laparoscopic repair are reported at 45–77 minutes; operating times for open herniorrhaphy are 37–45 minutes.<sup>45,52-55</sup>

Pain scores tend to be lower and length of hospital stay shorter for patients undergoing laparoscopic herniorrhaphy compared with open techniques.<sup>46,52,54</sup> In the immediate post-operative period, laparoscopic repair is found to be more painful than open repair with local anesthesia, but patients reported less pain 2 weeks postoperatively.<sup>56</sup>

Patient satisfaction indices after open and laparoscopic herniorrhaphy are generally very high for both procedures. The laparoscopic repair provides a better cosmetic result.<sup>57</sup> Length of disability after surgery also favors laparoscopy, in some cases by more than 2 weeks.<sup>46,52,54</sup> Short- and longterm measures have indicated a higher level of overall patient satisfaction with laparoscopic herniorrhaphy at 1, 4, 6, and 12 weeks.<sup>56,58</sup>

Open herniorrhaphy continues to be more costeffective than laparoscopic repairs, even when calculations for lost working days and disposable equipment are taken into account.<sup>52,56,58</sup> Over time and with increased experience, the difference in cost is far less than it initially appears. Estimates range from over \$500 to merely \$32.<sup>56,58</sup> However, cost is the primary reason that the National Institute for Clinical Excellence (NICE) did not recommend laparoscopy over open repair, but this report failed to consider factors that tend to ameliorate the cost difference.<sup>35</sup>



### *Conclusion*

Laparoscopic herniorrhaphy has rapidly developed into a procedure that rivals open surgical techniques in results, time and cost. As more physicians are trained in laparoscopy, the time of the procedure will more closely approximate that of open repair, and equipment improvements will further lower costs.

### **Ventral/incisional hernia**

#### *Diagnosis, work-up, and staging*

The key components in the diagnosis of a ventral or incisional hernia are not very different than for inguinal hernias. A thorough physical examination will often provide enough information for the surgeon to plan a repair. Ventral hernias are often associated with previous surgeries, obesity, or multiple pregnancies. In addition to abdominal wall incisional hernias, ventral abdominal wall hernias include spigelian, umbilical, and diastasis recti abdominis. The latter appears as a midline supraumbilical abdominal protuberance similar to incisional hernias. While the linea alba is wide, risk of incarceration and/or strangulation is low because no fascial defect is present. Spigelian hernia refers to a congenital or acquired protrusion of peritoneum at the lateral edge of the rectus muscle at the level of the linea semilunaris. The external oblique muscle overlies these hernias, obscuring the diagnosis. Umbilical hernias protrude through a persistent fascial defect at the level of the umbilicus. Particularly in obese patients but also in patients with an ambiguous physical examination, CT may confirm the presence of a ventral hernia.

#### *Indications and contraindications*

Many of the same contraindications for laparoscopic inguinal herniorrhaphy apply to laparoscopic ventral herniorrhaphy: specifically, known infection and cardiopulmonary compromise are relative contraindications for laparoscopic repair. Patients with multiple abdominal surgeries and known dense adhesions are at increased risk for bowel obstruction and injury and should be approached with caution. A large fascial defect extending beyond the midclavicular lines laterally may contraindicate laparoscopic repair, since space for trocar placement outside the margins of the hernia may be impossible. Proximity of the hernia defect near the xiphoid or symphysis pubis generally does not pose a problem. The preoperative preparation for laparoscopic ventral hernia repair is identical to that described for inguinal herniorrhaphy.

#### *Equipment and materials*

The laparoscopic instruments required to perform a ventral herniorrhaphy are identical to those needed for inguinal herniorrhaphy. The primary instrument that is not necessary for inguinal repair but is vital for ventral herniorrhaphy is a suture passing device with which the surgeon retrieves anchoring sutures to assure fixation of the prosthetic mesh to the anterior abdominal wall.

Several patch materials have been used in ventral hernia repair, including plastic, polyglycolic acid, polypropylene, polyester, and polytetrafluoroethylene (PTFE). After reports of enterocutaneous fistulas following intraperitoneal placement, use of intraperitoneal polypropylene mesh in transperitoneal laparoscopic hernia repair is contraindicated.<sup>59</sup> Although several authors contend that the danger of enteral complications due to polypropylene mesh is exaggerated,<sup>60–63</sup> credible evidence of intraperitoneal adhesions, small bowel obstruction, enterocutaneous fistulas, and mesh fibrosis is sufficient to deter use of polypropylene mesh within the peritoneal cavity.<sup>64</sup>

Fortunately, expanded polytetrafluoroethylene (ePTFE) offers several advantages over other materials, because its surface porosity can be varied to enhance ingrowth on the peritoneal aspect while limiting adhesions to bowel on the opposite side. Early ePTFE mesh had pore sizes greater than 17  $\mu$  which promotes ingrowth. Gore-Tex DualMesh Plus (WL Gore and Associates, Flagstaff, Arizona) with antibiotic impregnation, has pores that are less than 3  $\mu$ m on the intraperitoneal side, reducing visceral adhesions while the opposite side appears corrugated with a fibrinous microstructure that facilitates incorporation into the fascia.<sup>65</sup> The disadvantage of ePTFE compared with other materials is a bulkiness that makes it more difficult to manipulate intraoperatively, and some authors claim that its hydrophobic properties induce a higher incidence of seromas.<sup>66,67</sup>

### *Technique*

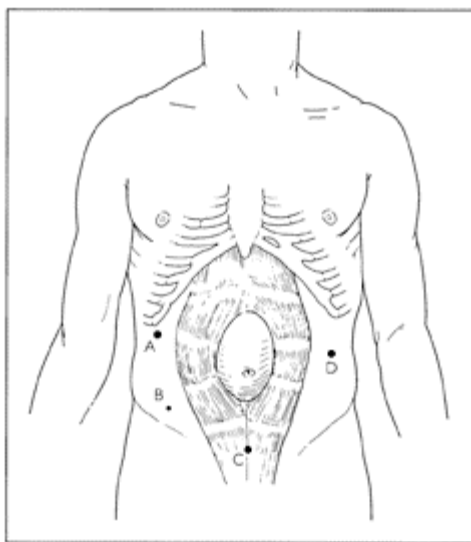
In ventral herniorrhaphy, proper trocar placement will facilitate the procedure. If possible, trocars should not be placed through previous incisions where scar impedes trocar insertion and underlying adhesions increase risk of bowel injury—conditions which favor placement of the first trocar under direct vision. Following entry into the peritoneal cavity, a finger sweeps nearby adhesions from the anterior abdominal wall to create a working space for the laparoscope. Fascial retention sutures elevate the fascial edges to permit inspection, secure the Hasson trocar to occlude loss of pneumoperitoneum, and provide fascial closure at the termination of the procedure. After placement of the trocar and insufflation of the peritoneal cavity, a 30° or 45° scope provides a direct view of the anterior abdominal wall and hernia during insertion of additional ports. Usually, a total of 3–4 ports are required to safely and efficiently perform laparoscopic ventral herniorrhaphy (Figure 24.11). With the advent of smaller staplers, only the scope port needs to be larger than 5 mm.

Placement of the camera in the midline facilitates dissection and fixation from either side of the table while avoiding a mirror image view. The costal margin can impede deflection of the laparoscope; inferior placement of the camera will avoid this problem. Furthermore, the laparoscope should be at least 6 cm from the nearest fascial edge to allow sufficient margin for mesh fixation. Working trocars are placed along the flanks with at least one on each side of the hernia to facilitate dissection and fixation.

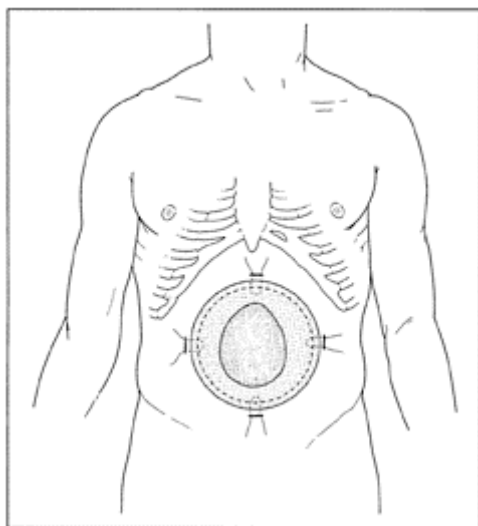
Occasionally, insufflation of the abdominal cavity alone will cause omentum or bowel to fall from the hernia sac; more often, however, meticulous dissection of adhesions in and around the defect is needed to reduce the hernia contents before placing mesh to cover the defect. Atraumatic graspers will safely provide traction and a Kitner dissector provide blunt dissection; avascular adhesions are divided sharply with scissors or with harmonic scalpel. Electrocautery is used with caution. The goal is a 4–5 cm margin of

fascia around the defect, providing ample space for mesh fixation. When repairing an incisional hernia, the entire incision must be covered by mesh—not just the obvious defect, as smaller defects along the old incision may go unrecognized. If only the small, visible defect is repaired with mesh, recurrence along the uncovered portion of the incision will likely occur.

Following reduction of hernia contents, the exact dimensions of the defect should be measured. A minimum of 4 cm should be added to these measurements to provide at least 2 cm overlap in all directions. Holzman advocates fashioning a circular piece of mesh whose diameter is 4 cm longer than the longest dimension of the defect; the circular configuration eliminates problems with orientation once the mesh is inserted into the abdomen<sup>68,69</sup> (Figure 24.12). If one chooses a more custom-fit (i.e. elliptical mesh) approach, corresponding points on the cut



**Figure 24.11** An example of port placement for repair of a large ventral hernia. The ports must be away from the fascial edge of the hernia in order to not interfere with mesh fixation with adequate overlap. The angled (30° or 45°) laparoscope is positioned in port site C to avoid mirror image phenomenon.



**Figure 24.12** Circular mesh eliminates orientation issues. Note the generous overlap with hernia fascial edge. Fixation sutures are placed at intervals around the mesh border prior to insertion into the abdomen. These sutures are then retrieved through small skin incisions one at a time using a suture retrieval device. Once the paired sutures are pulled through the skin incisions, the mesh is lifted into contact with the abdominal wall and the sutures tied.

mesh and abdomen can be marked with corresponding numbers, making correct orientation within the abdomen easier. In addition, for prostheses with different pore size on each side of the mesh—e.g. DualMesh Biomaterial—it is imperative to mark the mesh so that the proper side (small pore) is facing the peritoneal cavity.

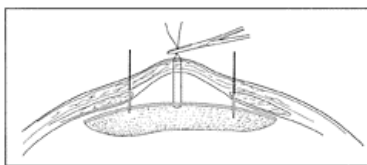
Prior to insertion, at least four nonabsorbable sutures should be placed through the mesh at equal intervals (see Figure 24.12). For very large patches, six or more nonabsorbable sutures should be placed along the perimeter. These sutures are left long and will be pulled up through the abdominal wall to firmly fix the mesh to the fascia. After cutting the mesh to size, we place the prosthesis on the abdominal wall and mark the skin at intended points of mesh fixation. We write a number on the mesh next to each suture and on the abdomen where each suture will be passed. This allows for quick orientation of the mesh once it is placed within the peritoneal space. We tightly roll the

mesh with the lateral and cephalad sutures tucked inside and the caudal suture left out. We pass the prosthesis through the 11 mm port with the caudal suture trailing. The mesh is unrolled and positioned with numbers aligned deep to the corresponding numbers marking the skin. A small stab incision (1–2 mm with No. 11 blade) pierces the skin at each of the numbered points. The ‘far’ side (away from the camera) of the mesh is fixed first. The suture passer enters the peritoneal cavity at an appropriate point and one end of the corresponding suture is withdrawn through the skin. The suture passer is reinserted through the same skin incisions, but pierces the fascia adjacent to the site from which the corresponding suture was withdrawn. The second paired suture is withdrawn through the skin and the two sutures are tagged together. This process is repeated around the circumference of the patch until all sutures have been drawn through the skin. The sutures are lifted, bringing the mesh into position against the abdominal wall, where inspection through the laparoscope should identify any inappropriate gaps between fixation sutures and/or inadequate margins between the fascial defect and the edge of mesh (Figure 24.13). Once the sutures are tied securely, staples or helical fixators are applied around the edge of the patch. The contralateral hand should be used to palpate the tip of the stapler prior to firing. This not only guarantees accurate placement of staples near the edge of the patch but also puts the abdominal wall and patch at a 90° angle to the stapler, which ensures good purchase for the staples (Figure 24.14). The edges of the mesh must not everte exposure of the large pores to the peritoneal contents will encourage adhesion formation with potential complications.

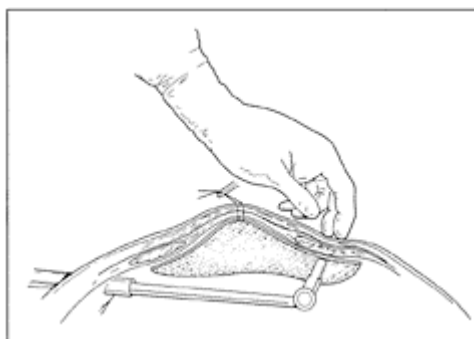
Once staples are applied at 1–1.5 cm intervals around the perimeter of the prosthesis, the patch should once again be inspected for gaps. Finally, all large trocars are removed and large (>10 mm) port sites closed with a suture-passing device using 2–0 PDS (polydioxanone surgical) sutures or with previously placed fascial retention sutures. Smaller trocar sites can be closed with a subcuticular absorbable stitch or simply with Steri-Strips.

### *Complications*

The most common complication reported for laparoscopic ventral hernia repair is a postoperative seroma which is reported in 4–25% of cases.<sup>64,66,70</sup> This fluid collection will resolve spontaneously in the majority of cases and aspiration should be avoided due to the risk of introducing bacteria into seroma.<sup>60,70</sup> In his review of 407 laparoscopic ventral herniorrhaphies, Heniford found only 2% of seromas remain 6 weeks following surgery.<sup>71</sup> Tsimoyiannis contends that seromas are routine and should be considered a complication only if they persist beyond 6 weeks, increase in size, or produce symptoms.<sup>70</sup> He suggests that cauterizing the hernia sac may decrease the incidence of postoperative seromas.



**Figure 24.13** Mesh is drawn up to the peritoneum, covering the fascial defect. Keith needles can be used to assess the overlap of the mesh along the fascial edges.



**Figure 24.14** Bimanual technique for applying helical staples. The nonoperating hand applies pressure to the abdominal wall to optimize staple placement by orienting the mesh and peritoneal staples at a 90° angle to the head of the stapler.

Major complications of laparoscopic herniorrhaphy are rare and include bowel enterotomies, mesh infection, enterocutaneous fistulas, necrosis of the overlying skin, and prolonged ileus. The reported incidence of bowel perforation is 1.0–1.5%.<sup>67,71</sup> Preoperative bowel preparation to reduce the bulk of the intraluminal contents as well as insertion of the initial trocar under direct vision help minimize the risk of bowel injury. Mesh infection always requires removal of the prosthesis; fortunately, the incidence of mesh infection and all other major complications is less than 1%.<sup>60,64,67,71</sup> Reports of enterocutaneous fistulas with ventral herniorrhaphy are exceedingly rare, and the initial concern that polypropylene mesh may be associated with a higher incidence of enterocutaneous fistulas appears unfounded.<sup>63</sup>

Other reported complications are infections of trocar site or along an anchoring suture, which occurred in 1.2–3.3% patients and are treated with oral antibiotics, and removal of

infected suture.<sup>60,64,67,71</sup> Several series reported postoperative hematomas, either at a trocar puncture site or at an anchoring suture, but only 1 patient required transfusion.<sup>65,66,71</sup> Heniford and associates found persistent suture pain lasting longer than 2 months in 2% of patients.<sup>71</sup>

### *Results*

Nearly all reports comparing laparoscopic ventral herniorrhaphy to open mesh herniorrhaphy found comparable recurrence rates.<sup>72</sup> Reported recurrence rates for laparoscopic ventral herniorrhaphy have ranged between 0 and 9%, with larger studies showing only 1–3% recurrence rate during nearly 2 year follow-up.<sup>60,67,71,73,74</sup> One randomized study showed significantly lower recurrence rate and morbidity for laparoscopic repair.<sup>73</sup> Both open and laparoscopic mesh repairs have fewer recurrences compared to open sutured repair.<sup>72</sup> The incidence of complications is comparable between open and laparoscopic approaches. Mean operating times ranged from 40 to 108 min.<sup>66,67,71</sup> Most series reported hospital stays from 1 to 4 days, although some reported large numbers of patients who were discharged the same day.<sup>66,67,70,71</sup> Postoperative pain is mild and typically lasts for only 1–2 days following surgery.

### *Conclusion*

The efficacy of laparoscopic herniorrhaphy is comparable and in some reports superior to open repair. The postoperative morbidity is less for the laparoscopic approach and the operating times and complication rates are similar. As further product development provides prostheses with greater tensile strength and lower rates of adhesion, this procedure should become the gold standard for ventral hernia repair.

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## Lower urinary tract symptoms (LUTS) and benign prostatic hyperplasia (BPH)

Matthew B Gretzer, Alan W Partin, and David Y Chan

### General description and epidemiology

Benign prostatic hyperplasia (BPH) is a non-neoplastic enlargement of the prostate gland that is highly prevalent among the aging male, and is characterized by a syndrome consistent with irritative as well as obstructive lower urinary tract symptoms (LUTS). While histologic evidence illustrates the development of hyperplastic nodules as early as 40 years old, the symptomatic effects of this process are more commonly exhibited by men in the fifth to eighth decade of life.<sup>1</sup> The risk of developing BPH doubles every year between the ages of 40 and 90, affecting 50% of men by 60 and up to 75% of men by 70 years of age.<sup>1,2</sup>

The high degree of prevalence of this disease is illustrated by its significant impact on the health care system within the United States with up to \$4 billion spent annually on evaluation and treatment.<sup>3</sup> Much of this expense may be attributed to the more than 200,000 surgical procedures performed each year on men with BPH. The exact cause of BPH has eluded ongoing research; however, new concepts have emerged that reveal that prostatic enlargement and the histologic hyperplasia may be components of a larger syndrome consisting of irritative and obstructive LUTS, diminished flow rate, and bladder outlet dysfunction.<sup>2</sup> With this in mind, the historic term prostatism is too simplistic, as these symptoms may not be specific to BPH or diseases of the prostate, and are more accurately described as LUTS (Table 25.1).<sup>2</sup>

### Etiology

Histopathologically, BPH is the result of hyperplasia of both epithelial and stromal cells within the periurethral transition zone of the prostate.<sup>4</sup> Whether the cause of this hyperplastic process is the result of epithelial and stromal proliferation or impaired cell death has yet to be defined.<sup>5,6</sup> The role of androgens, estrogens, stromal-epithelial interaction, and growth factors are believed to be significant contributors to this disease process.<sup>2</sup>

While androgens do not cause BPH, the development and maintenance of BPH require the presence of both testosterone and its active metabolite dihydrotestosterone (DHT) during puberty and aging.<sup>7</sup> This is evidenced by the lack of BPH in those men castrated

prior to puberty or among men affected with any of a variety of genetic diseases that impair androgen action or production.<sup>2,7</sup> Furthermore, androgen withdrawal has been illustrated to lead to partial involution of established BPH.<sup>8,9</sup> Thus, increasing age and a normal androgen-related hormonal axis are the most identifiable etiologic risk factors for the development of BPH. Aging is not only associated with increased receptor sensitivity to androgens but is also associated with elevated estrogen levels. These levels are increased either absolutely or relative in proportion to declining testosterone levels. Animal studies suggest that estrogens may sensitize the prostate to the effect of androgens, and that the imbalance of estrogens to androgens may contribute to a decrease in cell death within the aging prostate, leading to further prostatic growth.<sup>10,11</sup>

**Table 25.1** *Lower urinary tract symptoms (LUTS)*

| Irritative | Obstructive                 |
|------------|-----------------------------|
| Frequency  | Weak stream                 |
| Urgency    | Intermittancy               |
| Nocturia   | Hesitancy                   |
| Dysuria    | Sense of incomplete voiding |
|            | Post-void dribbling         |
|            | Straining to urinate        |

Testosterone is converted to its active metabolite by the enzyme 5-alpha reductase. Two versions of this enzyme have been identified.<sup>12</sup> Type 1 has been localized within the prostatic stromal cell. As DHT levels are maintained with aging, increased androgen receptor sensitivity permits further prostatic growth. Changing levels of DHT have been proposed to augment the effects of local growth factors within this stromal environment to impact the balance between cell proliferation and apoptosis.<sup>2</sup> The change in cellular milieu also brings about alterations in paracrine activity that affect the homeostasis between epithelial and stromal cells and contribute to the development of BPH.<sup>2,7</sup>

Several studies suggest that BPH also has an inheritable component.<sup>13</sup> Men less than 60 years old with large prostates (>37 g) and a first-degree relative requiring BPH-related surgery have up to a 4.2-fold increased risk of development of significant BPH.<sup>13</sup> The inheritance pattern for this finding suggests an autosomal dominant pattern, with as many as 50% of men undergoing surgery for BPH younger than 60 years old possessing this form of disease. Only 9% of men older than 60 years are thought to have a familial risk.<sup>13</sup>

### Pathophysiology

Complex forces contribute to the production of the LUTS observed in men with BPH.<sup>2,4,9</sup> Epithelial and stromal hyperplasia coupled with stimulation of the sympathetic innervation of the stromal elements produce outflow obstruction, yielding obstructive symptoms such as straining to void, weak stream, and hesitancy.<sup>4</sup> However, other forces must also be recognized as contributors to this disease process. Compensatory changes in bladder function as a result of this obstruction, compounded by age-related changes in bladder and nervous system function, lead to irritative symptoms (urgency, frequency, and nocturia), and are recognized as the most bothersome BPH-related complaints.<sup>2</sup>

Prostate size has not been found to correlate with the severity of LUTS, and it is becoming clear that these dynamic forces combined with bladder dysfunction probably play a significant role in the development of this disease process in older men.<sup>14</sup>

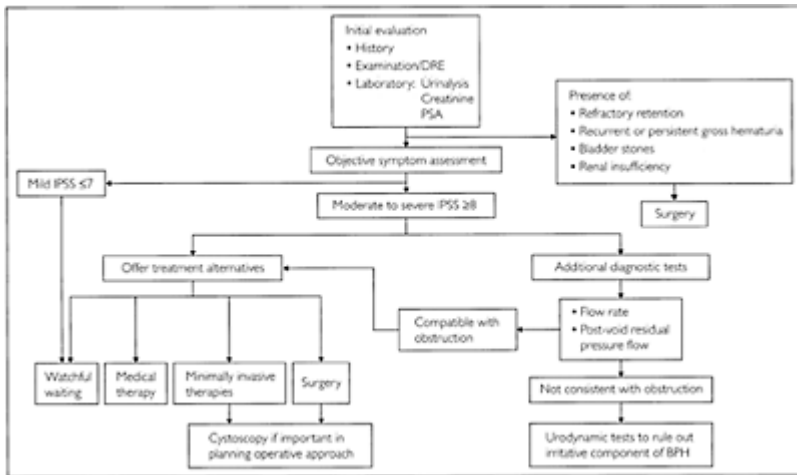
## Diagnosis

Due to the lack of specificity of these symptoms for BPH, other causes such as neurogenic bladder, urinary tract infection, urolithiasis, diabetes, urethral disease, and carcinoma (prostate or bladder) must first be excluded<sup>9</sup> (see Table 25.1). Fortunately, nonprostatic causes of these symptoms can be excluded in a majority of these patients on the basis of a detailed history, physical examination, and urinalysis. BPH guidelines have been published to aid the assessment of these patients (Figure 25.1).<sup>9,15</sup> The initial evaluation begins with a comprehensive medical history that focuses on the urinary tract, prior surgical procedures, and comorbid medical problems such as diabetes and hypertension. The physical examination consists of an abdominal examination, a digital rectal examination (DRE), and a complete neurologic examination to detect a palpable bladder, prostate, or rectal malignancy, to evaluate anal sphincter tone, and to rule out any neurologic problems that may mimic the presenting symptoms. The information from DRE on prostate size should not form the basis of treatment decision making, as prostatic size has not been shown to correlate with symptom severity or treatment outcomes.<sup>15</sup> Hyperplasia of the prostate tends to produce smooth, firm, and elastic enlargement of the prostate. BPH occurs within the transition zone of the prostate, a region not routinely palpated by the examining finger.

Urinalysis by dipstick or microscopic examination of sediment is performed to detect urinary tract infection or microscopic hematuria, which may indicate the presence of urothelial calculi or malignancy. Furthermore, in men with persistent or severe irritative symptoms, consideration for urine cytologic studies (even in the absence of hematuria) should be addressed to detect the presence of carcinoma in situ of the bladder. The measurement of serum creatinine is performed to rule out renal insufficiency. In the case of an elevated creatinine, renal ultrasound or intravenous pyelogram is warranted to check for upper urinary tract pathology. While prostate-specific antigen (PSA) measurement is optional in some BPH guidelines, screening should be offered to men beginning at 50 years old and at 45 years old for those with risk factors for prostate cancer (African-American or family history).

As a mode to assess a patient's baseline symptom complex prior to therapy, the American Urological Association has developed the International Prostate Symptom Score (IPSS) (Table 25.2).<sup>16-18</sup> In the AUA IPSS, symptoms are classified as mild (0-7), moderate (8-19), or severe (20-35). The IPSS should not be used to establish the diagnosis of BPH, but rather as a tool to grade baseline symptom severity, assess response to therapy, and to detect symptom progression in men managed by watchful waiting. Symptom scores may fail to capture the severity of these symptoms experienced by the individual patient; therefore, it may be more appropriate to treat a patient experiencing severe bother from moderate symptoms than a man with severe symptoms who describes his symptom complex as tolerable.

For men with moderate-to-severe symptoms (IPSS  $\geq 8$ ), additional testing recommended by the AHCPR (see Figure 25.1) includes urinary flow rate, post-void residual urine (PVR), and pressure-flow urodynamic studies.<sup>9,16,17</sup>



**Figure 25.1** Flow chart for work-up, evaluation and treatment of lower urinary tract symptoms (LUTS) and benign prostatic hyperplasia (BPH). DRE, digital rectal examination; PSA, prostate-specific antigen, IPSS, International Prostate Symptom Score.

While routine cystourethroscopy is not indicated in the absence of specific indications (hematuria), it is often performed prior to interventional therapy to assess the presence of bladder neck contracture, urethral stricture, and bladder tumors or calculi. It may also provide information regarding the prostatic urethra and presence of bladder outlet obstruction by a median lobe.

### Treatment

Treatment of BPH is based primarily on the presence of bothersome symptoms, and may be divided into four categories:

1. watchful waiting
2. medical management
3. minimally invasive therapies, and
4. surgical therapies.

Absolute indications for intervention include refractory urinary retention, recurrent severe urinary tract infection, gross hematuria due to BPH, and hydronephrosis or renal insufficiency secondary to BPH (Figure 25.1).<sup>2,7,9,15</sup> Optimal therapeutic planning should not only take into account the degree of symptom bother but also treatment efficacy and morbidity. While the goal of each therapy is symptom relief, the benefits of each of these various treatments must be tempered by the potential risk of complications (see Figure 25.2).

*Watchful waiting*

Watchful waiting may be an appropriate treatment strategy for many patients. Patients whose symptoms are mild or even moderate, but with a low degree of bother, may be managed with watchful waiting. BPH complications include urinary retention, renal insufficiency, urinary tract infections, gross hematuria, and bladder calculi. The probability of disease progression or the development of one of these complications during the course of watchful waiting has yet to be determined.<sup>9</sup> Until more information regarding the natural history of BPH is available, patients treated by delayed therapy, and medical therapy require periodic follow-up to monitor for changes in symptom level, physical findings, and laboratory values that would indicate the need for intervention.

**Table 25.2** *American Urological Association (AUA) index for benign prostatic hyperplasia (BPH)*

|   | AUA Symptom Index for BPH |                                |                               |                           |                               |                  |
|---|---------------------------|--------------------------------|-------------------------------|---------------------------|-------------------------------|------------------|
|   | Not<br>at all             | Less<br>than 1<br>time in<br>5 | Less<br>than half<br>the time | About<br>half the<br>time | More<br>than half<br>the time | Almost<br>always |
| 1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you have finished urinating? | 0                         | 1                              | 2                             | 3                         | 4                             | 5                |
| 2. Over the past month, how often than 2 hours after you have finished have you had to urinate again less urinating?                  | 0                         | 1                              | 2                             | 3                         | 4                             | 5                |
| 3. Over the past month, how often have you found you have stopped and started again several times when you have urinated?             | 0                         | 1                              | 2                             | 3                         | 4                             | 5                |
| 4. Over the past month, how often have you found it difficult to postpone urination?  | 0                         | 1                              | 2                             | 3                         | 4                             | 5                |
| 5. Over the past month, how often have you had a weak urinary stream?   | 0                         | 1                              | 2                             | 3                         | 4                             | 5                |
| 6. Over the past month, how often have you had to push or strain to begin urination?  | 0 0                       | 1 1                            | 2                             | 3                         | 4 4                           | 5                |

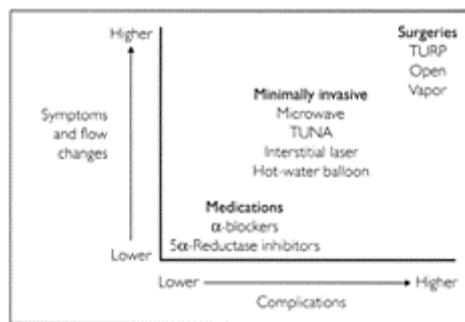
7. Over the last month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?

- |   |                 |
|---|-----------------|
| 0 | None            |
| 1 | 1 time          |
| 2 | 2 times         |
| 3 | 3 times         |
| 4 | 4 times         |
| 5 | 5 or more times |

Score=sum of questions 1–7 =

### Medical therapy

The introduction of medical therapies has had a tremendous impact on the management of BPH. Available medical therapies include alpha-adrenergic antagonists, 5-alpha reductase inhibitors, and phyto therapies. Doxazosin (Cardura), tamsulosin (Flomax), and terazosin (Hytrin) are the three most commonly prescribed alphaadrenergic antagonists, and act by relaxing prostatic stromal, capsular, and bladder neck smooth muscle (Table 25.3).<sup>18,19</sup> Alpha-blockers have no effect on serum PSA.<sup>19</sup> There is no evidence that one is more effective than another, and all have been shown to reduce symptoms up to 50%.<sup>18–21</sup> Short-term efficacy appears to be promising; however long-term results remain under investigation. Given the lack of alpha-adrenergic selectivity, both doxazosin and terazosin require dose titration to minimize the development of postural hypotension.<sup>21</sup> In the event these



**Figure 25.2** Graph of risk/benefit ratio of lower urinary tract symptoms (LUTS) vs complications of treatment. TURP, transurethral resection of the prostate; TUNA, transurethral needle ablation of the prostate.

medicines are interrupted, it is recommended that resumption of these drugs begin at the initial dosing regimen. Because tamsulosin is more specific for prostatic smooth muscle, it



may be added to pre-existing hypertensive therapy, and initiated and maintained at a dose of 0.4 mg/day.<sup>22</sup> Side-effects of alpha-blocker therapy include postural hypotension, drowsiness, dizziness, headache, and nasal congestion, and 10% of patients have been found to be unable to tolerate this form of medical therapy.<sup>18–21</sup> No evidence to date suggests that this class of medical therapy alone reduces BPH complication rates or the need for surgery.

Finasteride (Proscar) is a 5-alpha reductase inhibitor that prevents the conversion of intraprostatic testosterone to its active metabolite DHT.<sup>23</sup> This therapy has been associated with both a reduction in prostate size and IPSS score after a minimum of 6 months of therapy.<sup>24–26</sup> A recent study evaluating the long-term effects of medical therapy on the progression of BPH revealed a reduced risk of acute urinary retention as well as a decline by 60% in the requirement for invasive treatment (transurethral resection of the prostate or TURP) with long-term use of finasteride.<sup>26</sup> Additional data from another recent study report that symptomatic men with BPH who were treated with a combination of an alpha-blocker and finasteride showed significantly delayed clinical progression of their symptoms and significant improvements in symptom score and flow rate compared with treatment with each drug individually.<sup>27</sup> As finasteride causes a 50% reduction in serum PSA, men with elevated PSA levels should receive a complete prostate cancer evaluation prior to initiation of this therapy. Finasteride is generally well tolerated. Sideeffects include impotence (3%), decreased libido (3%), decreased ejaculate (2%), and minimal reports of breast tenderness and gynecomastia.<sup>23–26</sup>

Phytotherapies utilizing plant extracts continue to be a popular alternative therapy for the treatment of BPH.<sup>28</sup> The most popular herbal agent is *Serenoa repens* (saw palmetto), which is derived from the berry of the American dwarf palm tree. *Pygeum africanum* and betasitosterol are often used individually or in combination with saw palmetto by many patients with BPH. These compounds are exempt from the rigorous federal approval process, unlike conventional medical therapies in the USA. The resulting lack of standardization limits our understanding of the use and effectiveness of phytotherapy. Despite these shortcomings, emerging clinical trials report subjective and objective clinical improvement beyond placebo with minimal side-effects.<sup>29</sup> While the exact mechanism remains unknown, histologic evidence has

**Table 25.3 Medical and phytotherapy**

| Alpha-blocker  | 5- $\alpha$ -reductase inhibitor                  | Phytotherapy                                    |
|--|---|---|
| Doxazosin (Cardura) Start 1 mg qd with weekly stepwise titration to 2, 4, 8 mg/day PDR (54), p 2325  | Finasteride (Proscar) 5 mg po qd PDR (54), p 1876 | <i>Serenoa repens</i> (saw palmetto) 320 mg/day |
| Terazosin (Hytrin) Start 1 mg qd with weekly stepwise titration to 2, 5, 10 mg/day PDR (54), p 454   |   |   |
| Tamulosin (Flomax) 0.4 mg/day (no titration needed) PDR (54), p 801  |   |   |
| Alfuzosin (Xatral XL) Not available in the USA   |   |   |
| PDR, physician desk reference (54)=Progress in drug research, Vol. 54, E. Jucker, ed. Basel: Birkhauser Verlag, 2001. qd, every day; po, orally. |   |   |

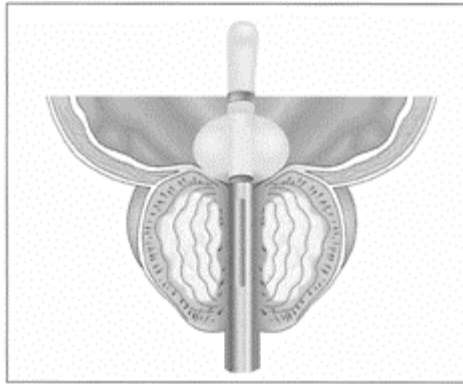
been presented that demonstrates atrophy and epithelial contraction in the prostate gland of men with BPH treated with saw palmetto.<sup>30</sup>

### *Minimally invasive therapies*

The last decade has brought about technical advances that have led to a surge in new minimally invasive treatment alternatives to TURP. Economic and societal forces have created a demand for less-invasive procedures that achieve durable symptomatic improvements without the morbidity of current surgical options or the side-effects and compliance issues associated with medical therapies. The underlying principle which all of these alternative therapies share is the production of coagulation necrosis of prostatic tissue by thermoablation using various kinds of energy, such as microwave, radiofrequency (RF), laser, ultrasound, and heated water.

### **Transurethral microwave therapy**

Transurethral microwave thermotherapy (TUMT) uses microwave energy in the range of 800–1300 MHz to heat and produce coagulative necrosis within the transition and central zone of the prostate. The production of coagulative necrosis depends on both the temperature achieved and the duration of heat exposure to the tissues. A catheter situated within the prostatic urethra is fitted with a microwave antenna. Microwave energy penetrates and radiates heat energy up to 7 mm (Figure 25.3). By simulta-



**Figure 25.3** Transurethral microwave thermotherapy (TUMT). A microwave antenna is fitted into a Foley catheter situated within the prostatic urethra. The microwave energy penetrates and radiates heat energy up to 7 mm of depth.

neously cooling of the penile and bulbar urethra, newer TUMT catheters are capable of not only preventing urethral sloughing from heat damage (improving tolerance of therapy) but also provide surface cooling that enhances microwave radiation and penetration of heat, thus achieving adequate coagulative necrosis of BPH tissue in shorter periods of treatment.<sup>31</sup> The design of the microwave antenna has also been shown to influence the distribution of energy to the prostate, and potentially affects the efficiency of therapy.<sup>32,33</sup> The two types of antenna currently available are the monopole and dipole antennae. When evaluating the heating patterns of these two antennae within a phantom, the monopole design displayed asymmetric heating and back heating of radiant energy along the antenna towards the energy source.<sup>33</sup> While this was elicited within a phantom experiment, this finding could potentially expose the external sphincter to excessive heat during therapy. The dipole antenna was not found to illustrate back heating, and in fact exhibited symmetrical distribution of heat energy. Furthermore, the dipole antenna was found to exhibit impedance matching with target tissue, which has been suggested to represent a feature suggestive of efficient delivery of thermal energy.<sup>33</sup>

While technical advancements have provided some improvement in therapeutic outcomes, optimal therapy will remain elusive until the 'intrinsic' factors of the prostate are better understood.<sup>34,35</sup> The heterogeneous tissue architecture of the BPH adenoma coupled with the presence of chronic inflammatory changes has been suggested to prevent attainment of optimal heating within the prostate.<sup>35,36</sup> Furthermore, the degree of intraprostatic vascularization seems to play an active role in determining the response to the thermal energy applied.<sup>34</sup> Known as the heat-sink phenomenon, the loss of thermal energy during treatment is often illustrated by the failure to achieve higher temperatures in the face of higher energy delivery, thus limiting optimal therapy.<sup>37,38</sup>

Many studies have documented both objective and subjective improvements in voiding following this therapy.<sup>31,39–41</sup> The symptomatic improvement appears to be energy-related, as outcomes have improved since devices have converted from low- to high-energy delivery.<sup>41</sup> In sham control studies, improvements in both IPSS and peak flow rates were observed 12 weeks after microwave therapy, suggesting that maximal improvement from TUMT is not achieved until 3 months after therapy.<sup>39</sup> Studies evaluating adjuvant therapy, combining an alphablocker with TUMT, reveal earlier symptom improvement is not obtained until 3–4 months, at which time TUMT demonstrates superior improvement in symptoms, voiding function, and quality of life compared to alphablockade.<sup>42</sup> Studies comparing TURP and TUMT have revealed subjective and objective improvements for both therapies, although the improvements are more pronounced after TURP.<sup>43,44</sup> However, complications were observed more frequently in the TURP group than with microwave therapy. Long-term efficacy studies have demonstrated that 67% of men treated with TUMT were without need for further therapy at 5 years.<sup>45</sup>

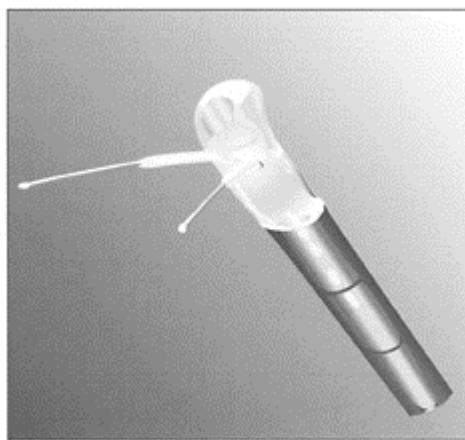
### **Transurethral needle ablation of the prostate**

Transurethral needle ablation of the prostate (TUNA) uses low-level RF energy delivered to the prostate parenchyma through needles inserted transurethrally (Figure 25.4). This therapy requires accurate needle placement to achieve effective outcomes<sup>46,47</sup> (Figure 25.5). While local anesthesia in the form of Xylocaine (lidocaine) jelly and intravenous

(IV) sedation may be sufficient for some patients, supplementary spinal or general anesthesia may be required to afford optimum results.

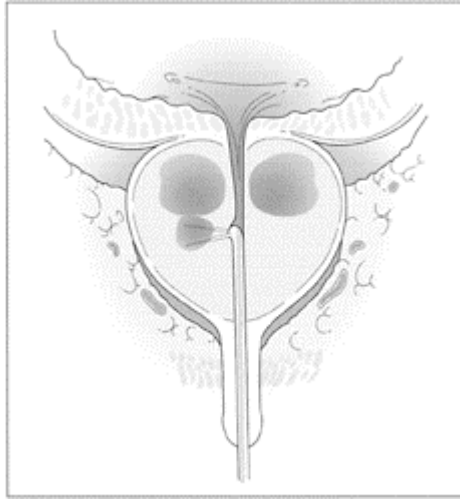
A monopolar RF signal of 490 kHz produces tissue heating due to tissue resistance to current as it flows from the active electrode to the indifferent or return electrode. The needles within the adenoma represent the active electrodes, and the RF current is concentrated within this area due to the small surface area of these electrodes, effectively allowing delivery of energy to a defined area of tissue (producing temperatures of 80–100°C). Insulation covers the electrodes as they penetrate the prostatic urethra and provides protection and prevents damage to the urethral mucosa; limiting the incidence of postprocedural irritative voiding complaints (Figure 25.6). During RF therapy, production of tissue desiccation produces an increase in tissue impedance (resistance). The resulting lesion is limited by the production of increased tissue resistance that occurs with excessive or prolonged therapy (Figure 25.7). Optimal treatment relies on accurate placement of needles as well as optimal energy selection that provides appropriate tissue impedance for the desired heating effect.<sup>46,47</sup> The RF energy of TUNA does not penetrate tissue well, and produces a higher temperature within the core of the tissue being treated. While this necrotic region is produced rapidly, the size and distribution is small, requiring multiple electrode placements in order to completely treat the entire BPH adenoma. Treatment time is determined by the number of lesions (averages about 5 min per lesion) (Figure 25.8).

A number of prospective randomized and nonrandomized multicenter studies have provided evidence of both subjective and objective improvements during early and long-term follow-up.<sup>48–50</sup> On average, AUA symptom scores improve by 77% and peak flow increases by 6 ml/s at 12-month follow-up.<sup>48–50</sup> Some studies suggest that the degree of obstruction may affect overall efficacy of treatment.<sup>51,52</sup> Men with mild-to-moderate obstruction were found to have better outcomes compared with men with severe obstruction. Outcomes appear to be durable, with

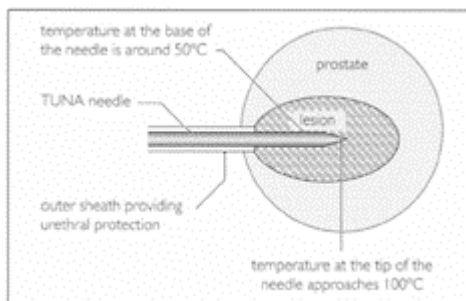


**Figure 25.4** Transurethral needle ablation of the prostate (TUNA) utilizes low-level radiofrequency

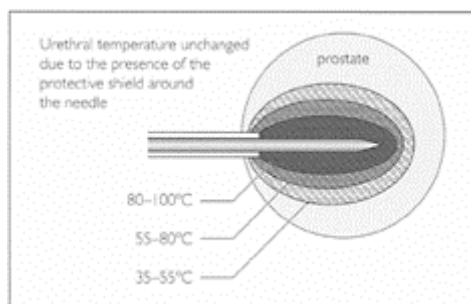
energy delivered to the prostate through needles inserted transurethraly.



**Figure 25.5** The TUNA<sup>TM</sup> procedure: accurate needle placement in the prostatic adenoma is required for optimal outcomes. (Reproduced with permission from Textbook of Benign Prostatic Hypertrophy. Edited by Roger Kirby, John D McConnell, John M Fitzpatrick, Claus G Roehrborn, and Peter Boyle. Chapter 36, page 424, Figure 36.1. Published by Isis Medical-Media Ltd, 1996, Oxford, UK.)



**Figure 25.6** TUNA™ procedure: the heating effect of the TUNA needle along the length of the needle. (Reproduced with permission from Benign Prostatic Hyperplasia Laser and Heat Therapy. Edited by Paul D Miller, Ian Eardley, and Steven A Kaplan. Chapter 12, page 132, Figure 12.1. Published by Martin Dunitz Ltd, 2001, London, UK.)



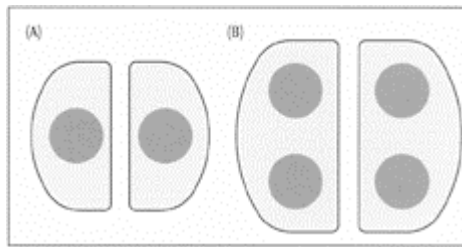
**Figure 25.7** TUNA™ procedure: tissue temperatures that are expected within the prostate with respect to the TUNA needle. (Reproduced with permission from Benign Prostatic Hyperplasia Laser and Heat Therapy'. Edited by Paul D Miller, Ian Eardley, and Steven A Kaplan. Chapter 12, page 132, Figure 12.2. Published by

Martin Dunitz Ltd, 2001, London, UK.)

reoperation rates of 10–15% at 2 years follow-up.<sup>53</sup> Most common adverse effects include transient retention in 13–41.6% of cases, and mild hematuria lasting 2 days.<sup>54</sup>

### Laser prostatectomy

Laser prostatectomy is another minimally invasive therapy that employs laser energy to produce coagulation or vaporization of prostate tissue through generation of temperatures ranging from 60°C to 90°C for coagulation and >100°C for vaporization. Laser variables such as wave-



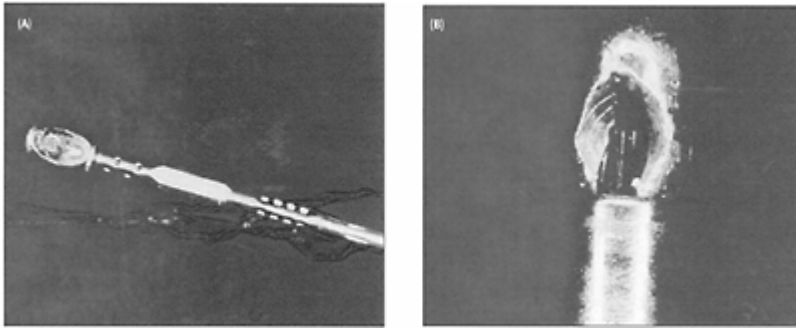
**Figure 25.8** Needle treatment is size dependent. (A) With small prostates, only a single pair of lesions in one plane is needed. (B) With larger prostates, two (or even three) planes of treatment are needed. (Reproduced with permission from Benign Prostatic Hyperplasia Laser and Heat Therapy. Edited by Paul D Miller, Ian Eardley, and Steven A Kaplan. Chapter 12, page 133, Figure 12.4a and b. Published by Martin Dunitz Ltd, 2001, London, UK.)

length and power, together with procedural variables (fiber motion) and tissue factors (vascularity, type of tissue), contribute to the overall laser tissue interaction observed for this mode of therapy. Currently available laser applications include sidefiring laser prostatectomy, interstitial laser prostatectomy (ILP), contact laser prostatectomy, and holmium laser resection of the prostate (HoLRP).

**Sidefiring laser prostatectomy.** This mode of laser therapy uses a sidefiring optical fiber to emit a beam into the prostatic adenoma<sup>55–57</sup> (Figures 25.9A and B). Wavelengths of

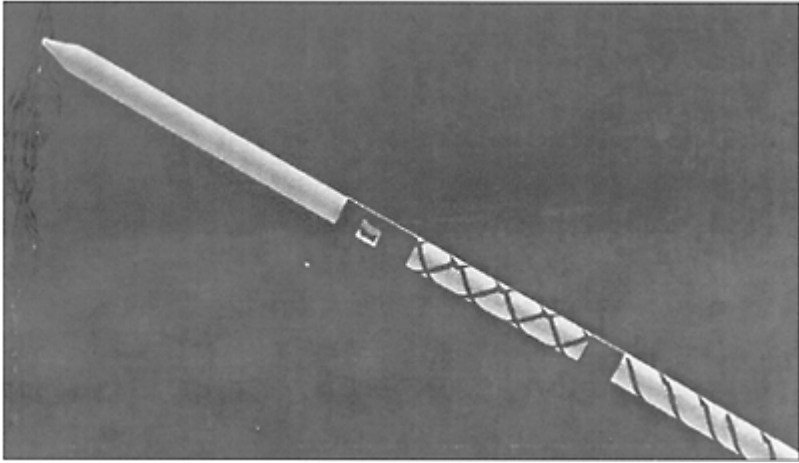
800–1100 nm (Nd:YAG and diode) are produced and are capable of penetrating tissue up to 15 mm in depth. Employing power setting of 40–60 W for 60s, this type of laser therapy produces coagulative necrosis of prostate tissue, which may take up to several weeks to slough. Using higher setting up to 90 W may provide for vaporization of tissue. Given the delayed necrosis and minimal blood loss, men with high American Society of Anesthesia (ASA) rating or those on anticoagulant therapy are best suited for this mode of therapy. While both AUA IPSS and flow rates have been shown to improve following this therapy over 3 years of follow-up (AUA IPSS 20.3 to 5.7,  $Q_{\max}$  7.3 to 18.5 ml/s), the prolonged time to maximum results has prevented wide acceptance of this mode of laser therapy.<sup>55–58</sup>

**Interstitial laser coagulation.** ILP is a minimally invasive therapy that also employs either an Nd:YAG or a diode laser energy to heat the prostate (Figure 25.10). During this procedure, a small fiber is inserted transurethraly or perineally into the prostatic adenoma using transrectal ultrasound guidance (Figures 25.11A and B). Once in place, the energy from the laser at low power



**Figure 25.9** (A and B): Bard Urolase beam-deflecting sidefire laser probe. Reproduced with permission from Benign Prostatic Hyperplasia Laser and Heat Therapy. Edited by Paul D Miller, Ian Eardley, and Steven A Kaplan. Chapter 5, page 55, Figures 5.7 and 5.8. Published by Martin Dunitz Ltd, 2001, London, UK.)

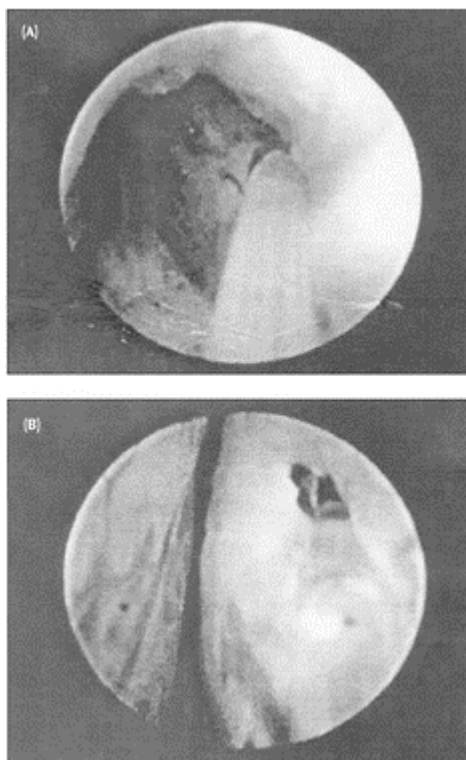




**Figure 25.10** Interstitial laser fiber—600  $\mu\text{m}$ , applicator 2 mm in diameter (Indigo, Cincinnati, Ohio). (Reproduced with permission from Benign Prostatic Hyperplasia Laser and Heat Therapy. Edited by Paul D Miller, Ian Eardley, and Steven A Kaplan. Chapter 8, page 80, Figure 8.5. Published by Martin Dunitz Ltd, 2001, London, UK.)

produces temperatures up to  $90^{\circ}\text{C}$  to yield coagulative necrosis. As the necrotic tissue remains intraprostatic, it is removed by tissue repair mechanisms. ILP produces spherical lesions up to 2 cm in diameter (Figures 25.12A-D). Thus, larger glands will require more treatments and longer overall treatment time.

Patient tolerance using both IV sedation and intraurethral Xylocaine or periprostatic block have been reported.<sup>59</sup> Improvement in both AUA symptom score and flow rates have been reported during short- and long-term follow-up.<sup>60-63</sup> One study of 394 patients reported sustained 3-year outcomes following Nd:YAG ILP with



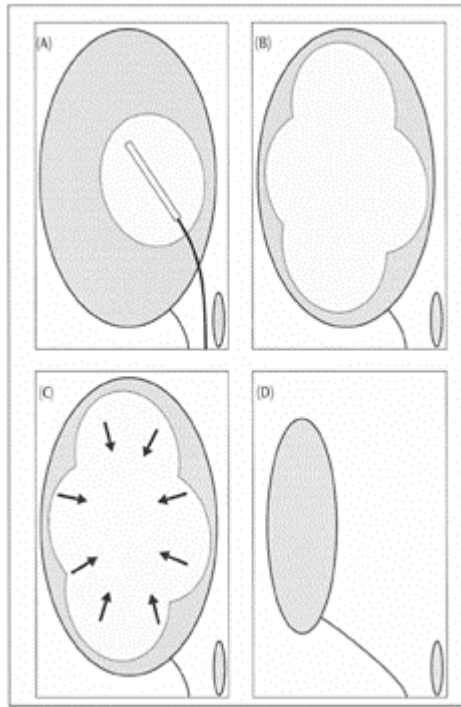
**Figure 25.11** Interstitial laser fiber placement: (A) in the 3 o'clock position of the left apex, fiber direction parallel to the table; (B) subsequent interstitial laser fiber placement in the 1–2 o'clock position of the left central lobe, fiber direction ventral.

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mean AUA score improvement from 24.2 to 7.9, while peak flow increased from 7.9 to 15.2.<sup>60</sup> Retreatment of this series was 16.3% over 3 years. Another study of 100 men following diode ILP also reports successful results at 1 year. AUA IPSS were found to

decrease from 22.4 to 8.3, with an increase of  $Q_{\max}$  from 8.6 to 14.2 ml/s.<sup>61</sup> The most common side-effect is dysuria, and postprocedural catheterization was required for up to 5 days.

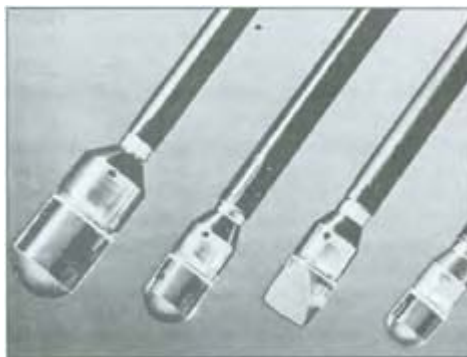
**Contact laser prostatectomy.** Contact laser therapy uses an Nd:YAG at high power (up to 90 W) to produce vapor



**Figure 25.12** Principle of interstitial laser coagulation of benign hyperplasia. (A) Interstitial laser treatment: where coagulation necrosis is generated within the prostatic adenoma without damage to the urethral surface. (B) Post-interstitial laser treatment: the intraprostatic adenoma lesion will atrophy. (C and D) Post-interstitial laser treatment: after intraprostatic atrophy, the prostatic lobes will contract secondary to tissue healing, with resultant regression of the prostate lobes and

decrease in adenoma size without tissue sloughing. (Reproduced with permission from Benign Prostatic Hyperplasia Laser and Heat Therapy. Edited by Paul D Miller, Ian Eardley, and Steven A Kaplan. Chapter 8, page 78, Figure 8.2a-d. Published by Martin Dunitz Ltd, 2001, London, UK.)

ization upon contact with the prostatic tissue (Figures 25.13 and 25.14) In one prospective study comparing contact therapy to TURP, similar outcomes in regard to AUA IPSS were demonstrated at 1 year and maintained at 3 years follow-up (56% improvement).<sup>64</sup> However, the trend for peak flow improvement was not maintained. Baseline  $Q_{\max}$  of 11.8 ml/s improved to 17.1 ml/s at 1 year and declined to 13.4 at 3 years follow-up for men treated with contact therapy. This resulted in a higher retreatment rate of 18% (vs 9% for TURP) at 3 years.<sup>64</sup> Potential advantages observed with this therapy are less blood loss



**Figure 25.13** Contact laser tips attached to laser fiber. (Reproduced with permission from Benign Prostatic Hyperplasia Laser and Heat Therapy. Edited by Paul D Miller, Ian Eardley, and Steven A Kaplan. Chapter 6, page 61, Figure 6.1. Published by Martin Dunitz Ltd, 2001, London, UK.)

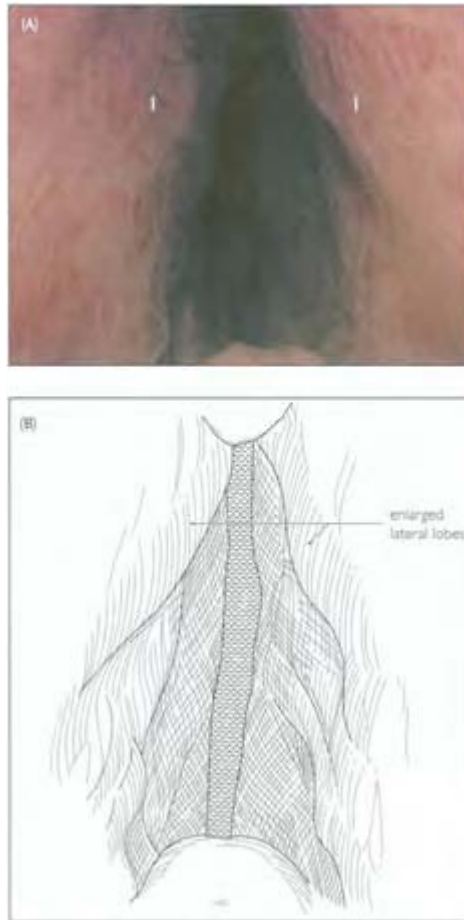


**Figure 25.14** Illustration of contact laser incising the bladder neck during a contact laser prostatectomy.

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and the use of saline irrigant, excluding the risk of TURP syndrome.

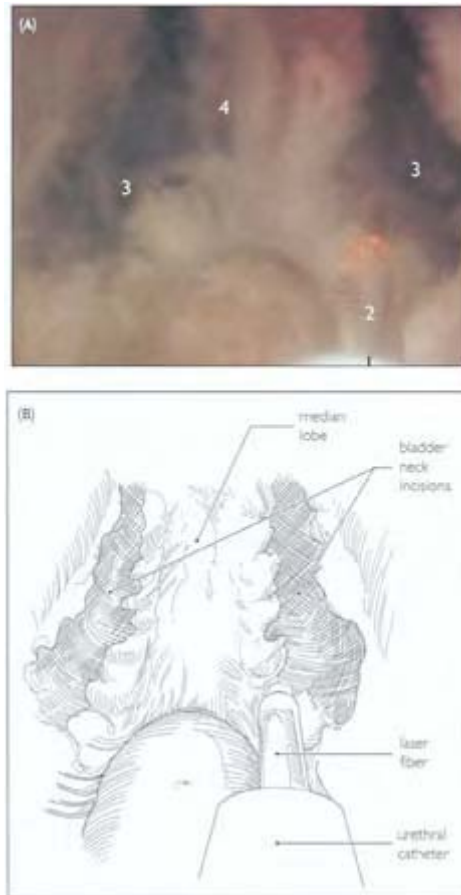
**Holmium laser prostatectomy.** Holmium laser resection produces thermomechanical vaporization, and can be used in a similar manner as TURP to resect large obstructing sections of adenomatous tissue. Once freed, these large sections of tissue are then fragmented and



**Figure 25.15** (A and B) Preoperative cystoscopy demonstrates lateral lobe enlargement (1) and high bladder neck. (Reproduced with permission from Benign Prostatic Hyperplasia Laser and Heat Therapy. Edited by Paul D Miller, Ian Eardley, and Steven A Kaplan. Chapter 9, page 97, Figure 9.1 (a and b). Published by Martin Dunitz Ltd, 2001, London, UK.)

removed through the working channel of a resectoscope. This technique is depicted with a series of pictures and illustrations (Figures 25.15–25.23).

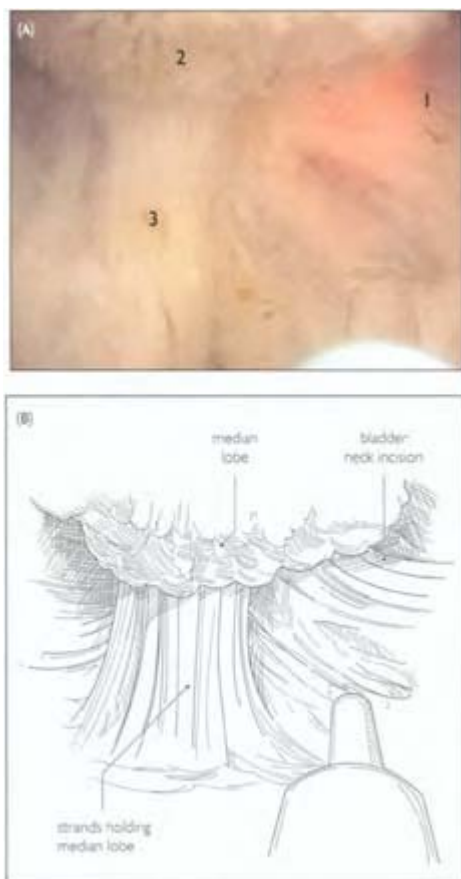
At 1 year AUA symptom scores improve by 65% and are similar to those following TURP (decrease of 21.9 to 4.2 for laser vs 23.0 to 4.3 for TURP).<sup>65,66</sup> Furthermore, peak flows were also similar, with  $Q_{\max}$  increasing from 8.9 to 25.2 for men treated by the laser and 9.1 to 20.4 following



**Figure 25.16** (A and B) Bladder neck incisions are made at 5 and 7 o'clock and taken down to the bladder neck fibers: 1=urethral catheter; 2=laser fiber; 3=bladder neck incision; 4=median lobe. (Reproduced with permission from Benign Prostatic Hyperplasia Laser and Heat Therapy. Edited by Paul D Miller, Ian Eardley,

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TURP. Retrograde ejaculation occurred in up to 80% of cases, and prolonged catheterization was not required by either group. As with TURP, experience with this procedure follows a prolonged learning curve. With the introduction of improved removal devices via morcellation, glands up to 100 g may be treated, and may offer an alternative to suprapubic prostatectomy as these devices mature.



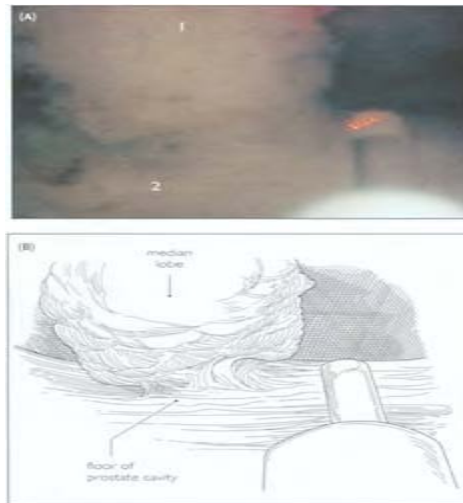
**Figure 25.17** (A and B) The fibrous attachments to the median lobes are incised between the two bladder neck incisions. (Reproduced with



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### High-intensity ultrasound

High-intensity ultrasound (HIFU) is another therapeutic option in treating BPH. The use of HIFU to cause tissue ablation has been successfully employed to treat lesions in the field of neurosurgery and ophthalmology.<sup>67,68</sup> This technique uses a transrectal ultrasound transducer for

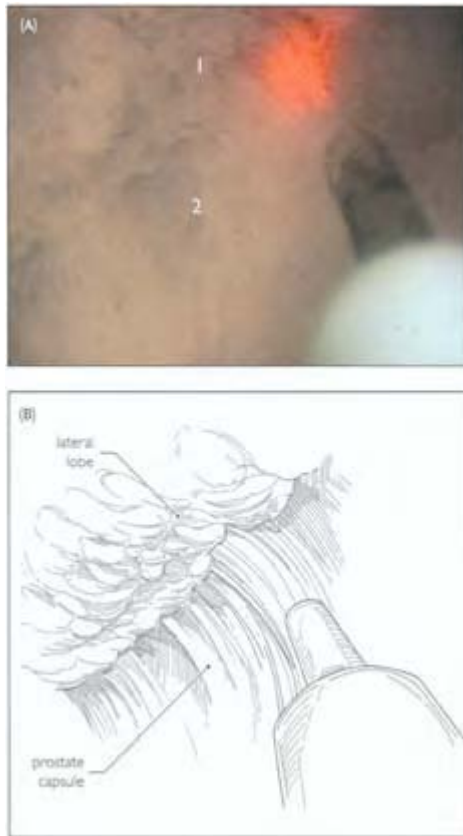


**Figure 25.18** (A and B) The last attachments of the median lobe are incised and the median lobe is pushed back into the bladder: 1=median lobe; 2=floor of prostate cavity.

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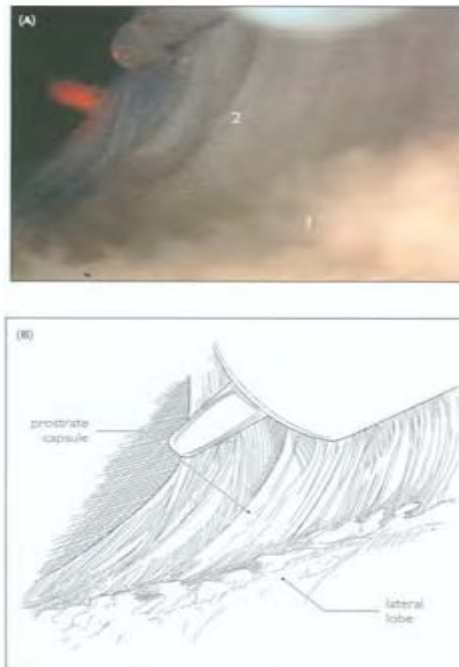
low-energy ultrasound imaging to deliver 4 s high-energy ablative ultrasonic pulses within a specific volume of prostatic tissue, achieving tissue temperatures of 80–100°C (Figure 25.24). Each cycle treats a region of tissue measuring approximately 40 mm<sup>3</sup>. Treatment begins at the bladder neck and continues circumferentially down to the verumontanum to create up to 8 tracts of treatment (Figure 25.25). Optimal treatment requires limited patient motion; thus epidural or general anesthesia is often



**Figure 25.19** (A and B) Release of the lateral lobe is accomplished by dissecting it off the prostatic surgical capsule: 1=lateral lobe; 2=prostate capsule. (Reproduced with permission from Benign Prostatic Hyperplasia

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required.<sup>69</sup> Large prostates greater than 80 g are not well suited, nor are prostates containing a median lobe. Due to significant prostatic urethral edema, urinary retention is often observed requiring prolonged catheterization of up to 1 week.<sup>69-71</sup> At 2 years follow-up, AUA symptom scores have been demonstrated to improve from 23 to 7, which compares well with TURP.<sup>70</sup> These symptomatic improvements are disproportionate to flow rates, which have not been observed to fare as well. While 12-month flow rates



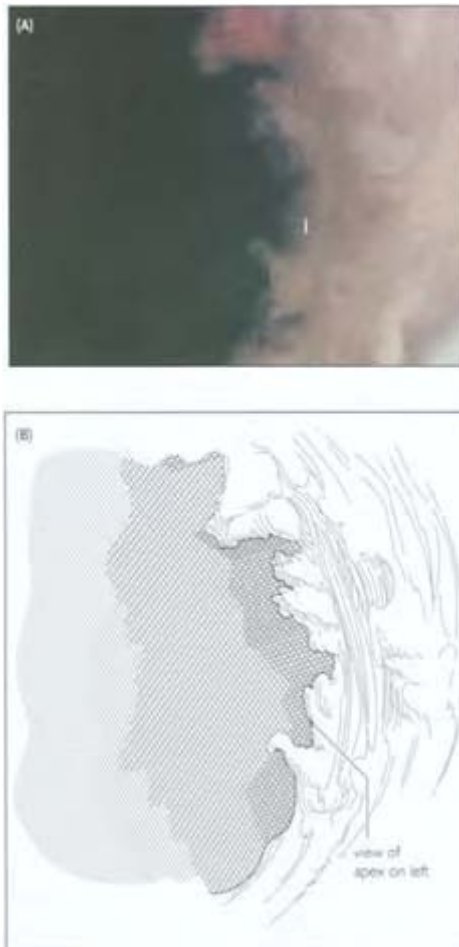
**Figure 25.20** (A and B) The upper portion of the bladder neck is extended to the prostatic surgical capsule. At this time the lateral lobe is separated from the surgical capsule: 1=lateral lobe; 2=prostate capsule. (Reproduced with permission from Benign Prostatic

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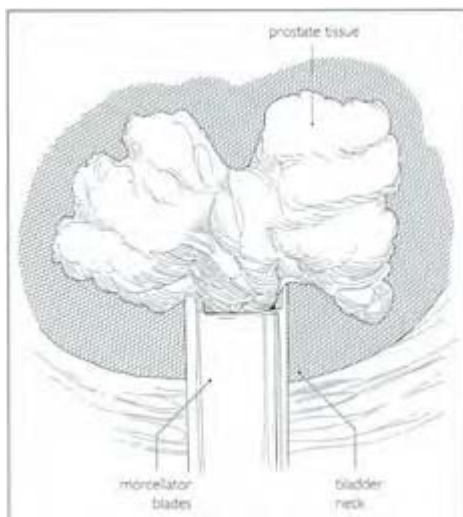
**Figure 25.21** (A and B) Enucleation of the lateral lobe is accomplished by connecting the lower apical incision to the bladder neck incision. The enucleated lobe is pushed back into the bladder: 1=bridge of tissue holding;

2=upper incision; 3=lower incision.  
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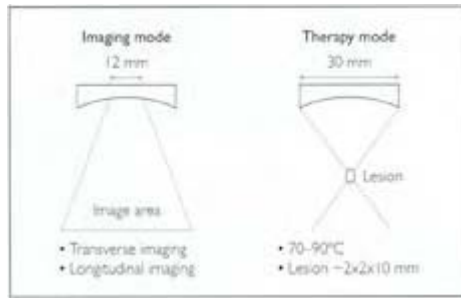


**Figure 25.22** (A & B) A barrel-shaped cavity is created by enucleation of the lateral lobes: 1=view of apex on left

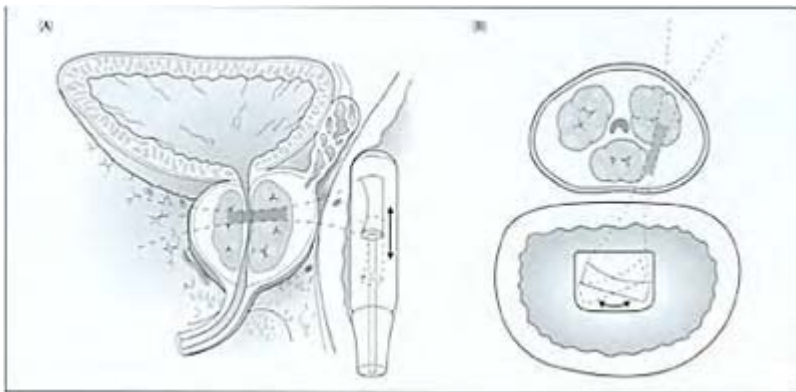
side. (Reproduced with permission from Benign Prostatic Hyperplasia Laser and Heat Therapy. Edited by Paul D Miller, Ian Eardley, and Steven A Kaplan. Chapter 9, page 100, Figure 9.8a and b. Published by Martin Dunitz Ltd, 2001, London, UK.)



**Figure 25.23** Tissue fragmentation takes place in a full bladder under direct cystoscopic vision. (Reproduced with permission from Benign Prostatic Hyperplasia Laser and Heat Therapy. Edited by Paul D Miller, Ian Eardley, and Steven A Kaplan. Chapter 9, page 101, Figure 9.9a. Published by Martin Dunitz Ltd, 2001, London, UK.)



**Figure 25.24** Both imaging and high-intensity frequency ultrasound modes are located on the same transrectal HIFU transducer. (Reproduced with permission from Textbook of Benign Prostatic Hyperplasia. Edited by Roger Kirby, John D McConnell, John M Fitzpatrick, Claus G Roehrborn, and Peter Boyle. Chapter 37, page 430, Figure 37.2. Published by Isis Medical Media Ltd, 1996, Oxford, UK.)



**Figure 25.25** Volume lesion is generated by transrectal HIFU, with each lesion measuring about  $40 \text{ mm}^3$ . By sequentially stalking volume lesions in a longitudinal (A) and transverse (B) mode, the prostatic

adenoma is ablated. (Reproduced with permission from Textbook of Benign Prostatic Hyperplasia. Edited by Roger Kirby, John D McConnell, John M Fitzpatrick, Claus G Roehrborn, and Peter Boyle. Chapter 37, page 431, Figure 37.3a and b. Published by Isis Medical Media Ltd, 1996, Oxford, UK.)

improve from 9.9 ml/s at baseline to 15.6 ml/s, these values deteriorate by 2 years to 10.6 ml/sec.<sup>70</sup> Long-term followup and corroboration by other series are needed.

### **Water-induced therapy**

Transurethral water-induced thermotherapy (WIT) is another relatively new technique for the treatment of BPH.<sup>72</sup> A catheter with a positioning and treatment balloon is placed within the prostatic urethra. Once in place, the treatment balloon is inflated to 50F to compress the prostatic adenoma, essentially reducing blood flow and thus limiting heat dissipation once treatment begins. Hot water heated to 60°C is then circulated within the balloon, transferring heat to the adenoma to produce coagulative necrosis. Most patients tolerate this procedure, requiring only intraurethral Xylocaine jelly. Urethral edema and sloughing following this procedure are concerns, as men undergoing this procedure often complain of irritative voiding. Limited studies reveal improved symptom scores and decreased post-void residuals.<sup>72</sup> However, durability and efficacy over sham and TURP have yet to be demonstrated. Furthermore, the development of urethral necrosis and subsequent irritative voiding complaints are concerning, as this new technique strives to find its place among the armamentarium of alternative therapies for BPH.<sup>72</sup>

### **Intraprostatic stents**

Endourethral stent placement has become an alternative therapy for men with urethral stricture, but has not been as useful for symptomatic BPH as a minimally invasive therapy.<sup>73-77</sup> The Urolume stent is the most commonly used stent in the USA, and consists of a braided mesh cylinder of high-strength alloy wire (Figure 25.26). The





**Figure 25.26** Urolume is a self-expanding braided mesh cylinder of highstrength alloy wire. (Reproduced with permission from Textbook of Benign Prostatic Hyperplasia. Edited by Roger Kirby, John D McConnell, John M Fitzpatrick, Claus G Roehrborn, and Peter Boyle. Chapter 40, page 455, Figure 40.1. Published by Isis Medical Media Ltd, 1996, Oxford, UK.)

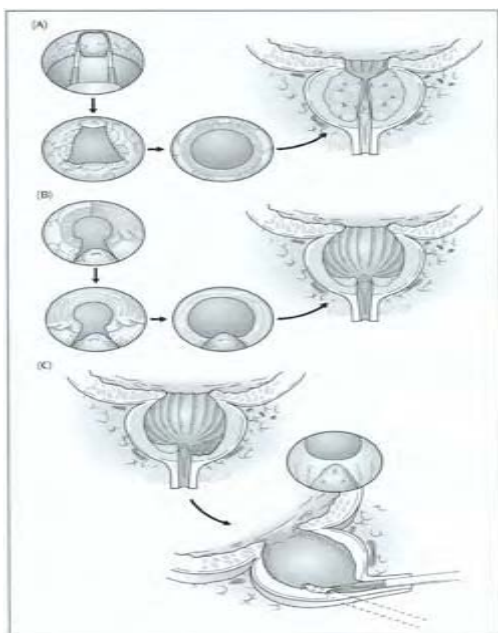
stent is placed into the prostatic urethra under direct visualization and is radially expanded after deployment (Figure 25.27). The procedure typically requires light anesthesia; however, spinal or local anesthesia can also be used. While



**Figure 25.27** Urolume delivery system placed the stent under direct vision into the prostatic urethra from the bladder neck to the verumontanum. (Reproduced with permission from Textbook of Benign Prostatic

Hyperplasia. Edited by Roger Kirby, John D McConnell, John M Fitzpatrick, Claus G Roehrborn, and Peter Boyle. Chapter 40, page 455, Figure 40.2. Published by Isis Medical Media Ltd, 1996, Oxford, UK.)

these stents have been found to be somewhat effective in relieving obstructive symptoms, reports of stent migration and erosion remain a concern, and have greatly limited use of such stents as a treatment for BPH.<sup>73,74</sup>



**Figure 25.28** Transurethral resection of the prostate (TURP; Nesbit technique). (A) Stage One—the median lobe, adjacent later lobe adenoma, and bladder neck fibers are resected. Resection is initiated at 12 o'clock and carried out circumferentially, completely resecting the bladder neck. (B) Stage Two—the adenoma is resected in quadrants. The

tip of the scope is positioned at the verumontanum and resection is started at 12 o'clock, resecting prostatic tissue from medial to lateral so that the lateral lobe falls into the middle of the prostatic fossa. Resection is taken down to the surgical capsule, which is identified by white glistening surface in contrast to the yellowish, nodular tissue of the adenoma. The upper right and left quadrants are resected first. The lower quadrants are then resected. Prostatic calculi are often an important landmark in this area and delineate the level of the surgical capsule. (C) Stage Three (resection of atypical adenoma)—The adenoma surrounding the verumontanum is resected. This tissue is located proximal to the external urinary sphincter. The tissue is resected from lateral to medial (verumontanum). (Reproduced with permission from Textbook of Benign Prostatic Hyperplasia. Edited by Roger Kirby, John D McConnell, John M Fitzpatrick, Claus G Roehrborn, and Peter Boyle. Chapter 31, page 345, Figure 31.2a-c Published by Isis Medical Media Ltd, 1996, Oxford, UK.)

### *Surgery*

Surgical management represents the oldest and most durable treatment for men with severe symptoms, or for men who do not respond to medical therapy. Standard surgical techniques include open prostatectomy, TURP (Figure 25.28), and transurethral incision of the prostate (TUIP) (Figure 25.29). Open prostatectomy is the oldest procedure, and is performed through a lower midline incision to allow complete, intact removal of the prostatic adenoma using either a suprapubic (through the bladder) (Figure 25.30) or retropubic (through the capsule of the prostate) (Figure 25.31) approach.<sup>75</sup> Open

prostatectomy has been shown to produce symptom improvements by as much as 98%; however, morbidity with open procedures and technological advancements have since limited this option to men with very large prostates (>70–100 g).<sup>75</sup>

The current reference standard for treatments utilized in the management of lower urinary tract symptoms secondary to BPH is TURP.<sup>76–78</sup> This technique is an electrosurgical procedure that uses a wire loop electrode to resect adenomatous tissue cystoscopically. Meta-analysis of various clinical studies reveal up to 88% symptom improvement following TURP.<sup>9,76–78</sup> Men with severe baseline bother have been shown to benefit the most from TURP.<sup>78</sup> Long-term studies illustrate good durability with low recatheterization and retreatment rates, and good satisfaction rates ranging from 75 to 87%.<sup>76–78</sup> Perioperative morbidities include TUR syndrome (hyponatremia resulting from absorption of irrigant), urinary tract infection, and failure to void. Potential longterm morbidities associated with this procedure include retrograde ejaculation (75%), impotence (1%), incontinence (1%), and bladder neck contractor (1%).<sup>76–78</sup> Transurethral electrovaporization of the prostate (TUV) is a technique very similar to TURP. This technique combines both electrosurgical vaporization and desiccation into one action. The dual nature of this electrode provides for accurate resection of tissue with limited blood loss. Trials comparing TUV to TURP have demonstrated equivalent short-term improvements in mean symptom score, quality-of-life score, peak flow rate, and post-void residual.<sup>79,80</sup> Advantages over TURP include minimal intraoperative and postoperative bleeding, as well as shorter catheterization and hospital stay. Disadvantages include lack of a tissue specimen for cancer diagnosis and slightly longer operative times.<sup>79,80</sup>

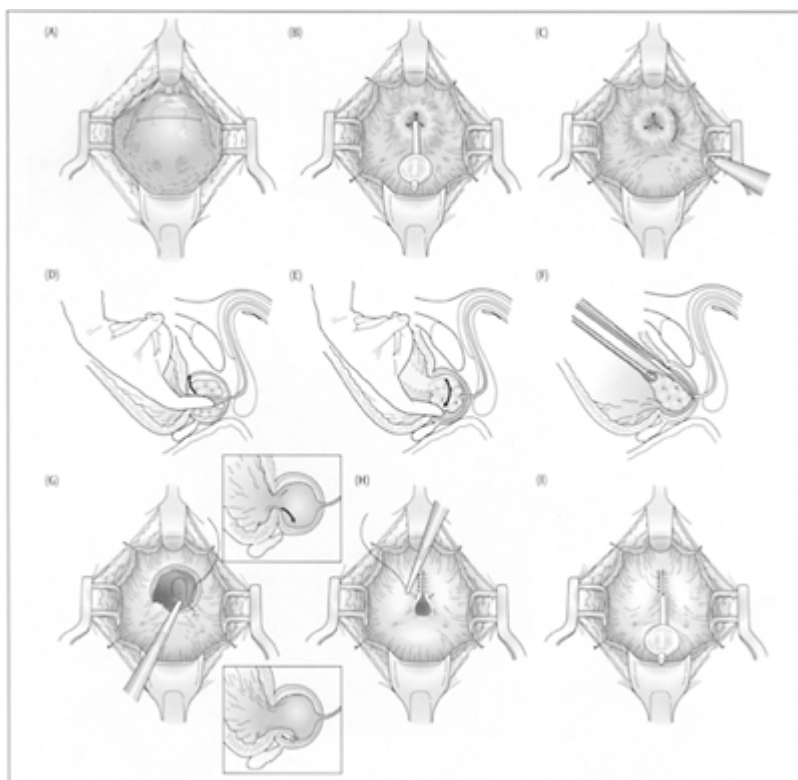
Transurethral incision of the prostate (TUIP) is a relatively simple surgical procedure that involves dividing the prostatic capsule at the bladder neck to redirect the compressive force of the hyperplastic tissue away from the urethra, effectively allowing the prostatic urethra and bladder neck to 'spring open'.<sup>81, 82</sup> TUIP may be performed in less time than TURP, and is associated with a lower incidence of bleeding and retrograde ejaculation. Optimal results for this procedure have been found in men with small prostates (<30 g).<sup>81–83</sup> TUIP has exhibited efficacies approaching TURP with low morbidity; however, it remains an underutilized procedure in the BPH therapeutic armamentarium.<sup>81–83</sup>

## Conclusion

BPH is a common condition that affects most men. Technological advancements, better pharmacologic treatments, and an improved understanding of the natural history of this disease have improved diagnosis and the options for therapeutic interventions. The degree of bother attributed to LUTS should provide the basis for selection of therapeutic options, including watchful waiting. Those with mild-to-moderate symptoms with minimal bother may be candidates for watchful waiting, whereas men with



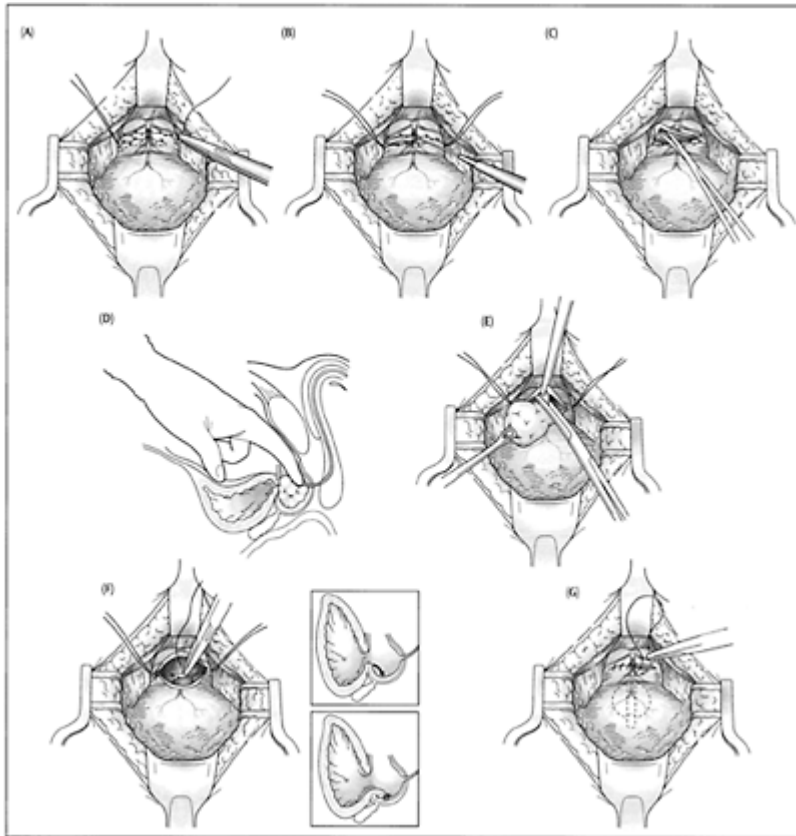
**Figure 25.29** Transurethral incision of prostate (TUIP)—Incision(s) are made from inside the bladder neck to the verumontanum down through prostatic capsule. Either a single incision is made at 6 o'clock or two incisions are made at 5 and 7 o'clock. (Reproduced with permission from *Textbook of Benign Prostatic Hyperplasia*. Edited by Roger Kirby, John D McConnell, John M Fitzpatrick, Claus G Roehrborn, and Peter Boyle. Chapter 31, page 344, Figure 31.1. Published by Isis Medical Media Ltd, 1996, Oxford, UK.)



**Figure 25.30** Suprapubic prostatectomy. (A and B) Exposure of anterior surface of bladder—a urethral catheter is positioned within the bladder on the sterile field and the bladder is distended with saline and the catheter is clamped. A lower midline or Pfannenstiel incision is made and the space of Retzius is exposed. A transverse incision is made through the anterior bladder wall. Stay sutures of 2–0 silk are placed on the bladder and secured to the rectus fascia. A self-retaining retractor is placed within the bladder to expose the bladder neck. (C) The bladder mucosa at bladder neck is incised circumferentially about 1.0–1.5

cm from urethra. (D) The anterior prostatic commissure is disrupted by inserting a finger in the urethral meatus and moving the finger upward forcefully. (E) Digital enucleation of the adenoma by manually dissecting between the adenoma and surgical capsule. (F) Division of the urethra is accomplished sharply with right-angled scissors. This maneuver will free the adenoma specimen. (G) After removal of the adenoma, bleeding is controlled by placing two figure-of-eight sutures at the 5 and 7 o'clock positions. To avoid a 'lip' at the bladder neck, these sutures incorporate the posterior portion of the prostatic fossa. This maneuver will allow a straight path to the bladder during urethral catheterization. (H) The bladder neck is reconstructed with 2–0 chromic. All prostatic fossa bleeders are controlled by direct electrocautery coagulation or suture ligator. (I) The procedure is finished by placing a suprapubic tube through a separate stab incision and closing the bladder in two layers with an absorbable suture. A closed suction drain is placed in the space of Retzius and the fascia and skin are closed in standard fashion. (Reproduced with permission from Textbook of Benign Prostatic Hyperplasia. Edited by Roger Kirby, John D McConnell, John M Fitzpatrick, Claus G Roehrborn, and Peter Boyle. Chapter 31, page 346, Figure 31.3a-i. Published by Isis

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**Figure 25.31** (A) The space of Retzius is exposed through a midline or Pfannenstiel incision. The anterior surface of the prostate is exposed with a self-retaining retractor. The dorsal venous complex is secured by placing two horizontal rows of sutures approximately 0.5–1.0 cm apart. (B) The prostatic capsule is opened anteriorly between the row of sutures with electrocautery. (C and D) Using curved-tipped scissors the plane



between the surgical capsule and adenomatous tissue is developed. Alternatively, the adenoma can be enucleated out of its capsule. (E) After enucleation, the urethra is transected with right-angled scissors. The adenoma is freely mobile and is extracted from the capsule incision with ring forceps. (F) After enucleation, bleeding is controlled with two figure-of-eight sutures at 5 and 7 o'clock at the bladder neck. The posterior bladder neck is sutured to the posterior prostatic fossa. All remaining bleeding is controlled by electrocautery or suture ligation. (G) The prostate capsule is closed with a 2-0 absorbable suture. The space of Retzius is drained with a closed suction drain. (Reproduced with permission from Textbook of Benign Prostatic Hyperplasia. Edited by Roger Kirby, John D McConnell, John M Fitzpatrick, Claus G Roehrborn, and Peter Boyle. Chapter 31, page 349, Figure 31.4a-g. Published by Isis Medical Media Ltd, 1996, Oxford, UK.)

significant bother may proceed to medical or minimally invasive interventional therapies (see Figure 25.2). While surgery remains the gold standard mainstay of these therapies, with the most durable results, outcomes for minimally invasive alternative therapies are encouraging and are rapidly becoming popular alternatives in the BPH armamentarium.

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## 26

# Urinary calculi: pathogenesis, metabolic evaluation, and medical therapy

Yair Lotan and Margaret S Pearle

### Introduction

Nephrolithiasis is a common disorder, with an approximate incidence of 0.4–1% and a prevalence of 5–12%.<sup>1</sup> Environmental, metabolic, and genetic factors have been implicated in stone formation, and an effort has been made to identify risk factors in individual patients in order to institute appropriate preventive measures. Although minimally invasive and noninvasive surgical treatments such as shock wave lithotripsy, ureteroscopy, and percutaneous nephrostolithotomy offer efficacious treatment options, they neither negate the morbidity associated with an acute stone episode nor resolve the underlying causes of stone formation. On the other hand, stone recurrence after surgical therapy can be reduced with appropriate medical therapy.<sup>2,3</sup>

In this chapter, we review the pathogenesis of stone formation and provide guidelines for the metabolic evaluation and medical and dietary treatment of nephrolithiasis.

### Pathogenesis

Calcium is the most common component of stones, occurring in nearly 75% of cases. Among the calcium-containing stones, calcium oxalate occurs most frequently (60% of all stones), followed by hydroxyapatite (20%) and brushite (2%). Uric acid and struvite (magnesium ammonium phosphate) each account for approximately 7% of stones, followed by cystine, at 1–3%. Several rare stone types, such as triamterene, adenosine, silica, indinivir and ephedrine, comprise the remainder.

Stones are classified according to the underlying metabolic or environmental abnormality with which they are associated. Calcium stones may be associated with multiple metabolic abnormalities, including hypercalciuria,<sup>4</sup> hypocitraturia,<sup>5,6</sup> hyperuricosuria, and hyperoxaluria, that can occur in isolation or in combination. On the other hand, uric acid, cystine, and struvite stones are associated primarily with a single metabolic abnormality; uric acid stones form only in an acid urine,<sup>7,8</sup> cystine stones are the result of impaired renal reabsorption of cystine,<sup>9–12</sup> and infection stones occur in an alkaline urine produced by urease-producing bacteria.<sup>10</sup> An understanding of the underlying metabolic disorders and environmental factors that predispose to stone formation makes possible the implementation of a rational treatment plan.<sup>13,14</sup>

*Hypercalciuria*

The role of hypercalciuria in stone formation is not established. However, several lines of evidence support a pathogenetic role. First, hypercalciuria is common in stoneforming patients, occurring in 35–65% of patients.<sup>15,16</sup> In addition, treatment aimed at reducing urinary calcium levels results in a reduction in stone recurrence rates.<sup>17–19</sup> Finally, medical therapy often fails in patients with persistent hypercalciuria.<sup>20</sup>

High urinary calcium concentrations lead to increased urinary saturation of calcium salts<sup>21</sup> and reduced urinary inhibitory activity associated with negatively charged inhibitors such as citrate and chondroitin sulfate.<sup>4</sup> Hypercalciuria is classified as absorptive, renal, or resorptive on the basis of the underlying pathophysiologic abnormality leading to the hypercalciuria, and treatment is ideally directed at correcting the underlying metabolic derangement.

Absorptive hypercalciuria (AH) is defined by increased urinary calcium excretion ( $>0.2$  mg/mg creatinine) after an oral calcium load. Although fasting urinary calcium is usually normal in AH ( $<0.11$  mg/100 ml glomerular filtration), severe forms of AH occasionally may be associated with fasting hypercalciuria as well. The underlying pathophysiologic abnormality in AH is increased intestinal absorption of calcium, which occurs in approximately 55% of stone formers.<sup>16</sup> AH is classified as Type I when urinary calcium remains high despite a low calcium diet (400 mg dietary calcium daily) and Type II when urinary calcium normalizes with restricted calcium intake. The added systemic load of calcium results in a transient increase in serum calcium, which suppresses serum parathyroid hormone (PTH) and results in increased renal filtration of calcium, ultimately leading to hypercalciuria. Because the increase in intestinal absorption of calcium is matched by enhanced renal calcium excretion, serum calcium remains normal.

The cause of increased intestinal absorption of calcium has been variously ascribed to vitamin D-independent and dependent processes, as well as to up-regulation of the vitamin D receptor.<sup>22</sup> However, no proposed mechanism completely accounts for all findings associated with absorptive hypercalciuria, and recent genetic studies have identified an unrelated gene associated with the absorptive hypercalciuria phenotype.<sup>23</sup>

In renal hypercalciuria, impaired renal tubular reabsorption of calcium results in elevated urinary calcium levels and subsequent secondary hyperparathyroidism.<sup>24</sup> Serum calcium remains normal because the renal loss of calcium is compensated for by enhanced intestinal absorption of calcium and bone resorption as a result of increased secretion of PTH and  $1,25\text{-(OH)}_2$  vitamin D. High fasting urinary calcium levels ( $>0.11$  mg/100 ml glomerular filtration) are characteristic of renal hypercalciuria.

Resorptive hypercalciuria is an infrequent abnormality that is most commonly associated with primary hyperparathyroidism. Excessive PTH secretion from a parathyroid adenoma leads to bone resorption and increased renal synthesis of  $1,25\text{-(OH)}_2$  vitamin D, which in turn enhances intestinal absorption of calcium; the net effect is elevated serum and urine calcium. Although most patients demonstrate hypercalcemia and hypercalciuria, in some cases normal serum calcium is associated with an inappropriately high serum PTH. Additional, rare causes of resorptive hypercalciuria include hypercalcemia of malignancy, sarcoidosis, thyrotoxicosis, and vitamin D toxicity.

### *Hyperuricosuria*

Hyperuricosuria, defined as urinary uric acid >600 mg daily, is the only abnormality detected in up to 10% of calcium stone formers.<sup>16</sup> Hyperuricosuria predisposes to calcium or uric acid stone formation by causing supersaturation of the urine with respect to monosodium urate. At pH <5.5, the undissociated form of uric acid predominates, leading to uric acid stone formation. At pH >5.5, sodium urate formation promotes calcium oxalate stone formation through heterologous nucleation.<sup>25</sup> In addition, uric acid crystals may reduce the inhibitory activity of urinary glycosaminoglycans (GAGs) against the crystallization of calcium oxalate.<sup>25</sup>

The most common cause of hyperuricosuria is increased dietary purine intake, since uric acid represents the end product of purine metabolism. However, acquired and hereditary diseases that may be accompanied by hyperuricosuria include gout, myelo- and lymphoproliferative disorders, multiple myeloma, secondary polycythemia, pernicious anemia, hemolytic disorders, hemoglobinopathies and thalassemia, complete or partial hypoxanthineguanine phosphoribosyltransferase deficiency, superactivity of phosphoribosylpyrophosphate synthetase, and hereditary renal hypouricemia.<sup>8</sup>

### *Hypocitraturia*

Citrate inhibits calcium stone formation by several mechanisms. First, citrate complexes with calcium, thereby reducing urinary saturation of calcium salts.<sup>26</sup> In addition, citrate directly prevents spontaneous nucleation of calcium oxalate<sup>27</sup> and inhibits agglomeration of calcium oxalate crystals<sup>28</sup> as well as growth of calcium oxalate and calcium phosphate crystals.<sup>29</sup>

Hypocitraturia is defined as urinary citrate < 320 mg daily. Urinary citrate excretion is determined primarily by the acid-base state. In states of metabolic acidosis, urinary citrate is reduced as a result of enhanced renal tubular reabsorption and decreased synthesis of citrate in peritubular cells.<sup>30</sup> Low urinary citrate results from a variety of pathologic states associated with acidosis. Distal renal tubular acidosis (RTA) is characterized by high urine pH (>6.8), high serum chloride, and low serum bicarbonate and potassium.<sup>31</sup> RTA is confirmed by demonstrating an inability of the urine to acidify in response to an oral acid load. Chronic diarrheal states produce hypocitraturia by causing systemic acidosis as a result of intestinal alkali loss in the stool.<sup>32</sup> Thiazide therapy induces hypokalemia and intracellular acidosis.<sup>33</sup> Excessive animal protein provides an acid load.<sup>34</sup> Lastly, lactic acidosis may occur during strenuous exercise.<sup>27</sup> However, hypocitraturia may also represent an isolated abnormality unrelated to an acidotic state.

Citrate levels in the urine increase in alkalotic states, as well as with elevated levels of PTH, estrogen, growth hormone, and vitamin D.

### *Hyperoxaluria*

Hyperoxaluria (urinary oxalate >40 mg/day) leads to increased urinary saturation and crystallization of calcium oxalate. The causes of hyperoxaluria include disorders in biosynthetic pathways; intestinal malabsorptive states associated with inflammatory



bowel disease, celiac sprue, or intestinal resection; and excessive dietary intake or high substrate levels of vitamin C.

Primary hyperoxaluria results from a rare autosomal recessive disorder in glyoxylate metabolism by which the normal conversion of glyoxylate to glycine is inhibited, leading to preferential oxidative conversion of glyoxylate to oxalate, an end product of metabolism. Consequently, markedly high urinary levels of oxalate ensue ( $>100$  mg/day), causing increased saturation of calcium oxalate and stone formation and severe nephrocalcinosis. Without treatment, end-stage renal failure is inevitable and occurs by age 15 years in 50% patients, with an overall death rate of approximately 30%.<sup>35</sup>

The most common cause of acquired hyperoxaluria is enteric hyperoxaluria, typically associated with chronic diarrheal states, by which fat malabsorption results in saponification of fatty acids with divalent cations such as calcium and magnesium, thereby reducing calcium oxalate complexation and increasing the pool of available oxalate for reabsorption.<sup>36</sup> In addition, the poorly absorbed fatty acids and bile salts are thought to further increase colonic permeability to oxalate.<sup>37</sup> Factors in addition to hyperoxaluria that contribute to calcium oxalate stone formation in chronic diarrheal states include dehydration, hypokalemia, hypomagnesuria, hypocitraturia, and low urine pH.

Hyperoxaluria in the absence of intestinal disease is commonly due to dietary overindulgence in oxalate-rich foods such as nuts, chocolate, brewed tea, spinach, broccoli, strawberries, and rhubarb. In addition, severe calcium restriction may result in reduced intestinal binding of oxalate and increased intestinal oxalate absorption. Ascorbic acid supplementation has been shown to increase urinary oxalate levels by in-vivo conversion to oxalate,<sup>38</sup> although increased clinical rates of stone formation have not been unequivocally linked to ascorbic acid use.<sup>39,40</sup> Recent studies have also implicated *Oxalobacter formigenes*, an oxalate-degrading intestinal bacterium, as a potential contributor to increased intestinal oxalate levels and subsequent elevated oxalate absorption in some stone formers.<sup>41,42</sup>

### *Hypomagnesuria*

Hypomagnesuria leads to reduced complexation of magnesium with oxalate, leading to increased urinary saturation of calcium oxalate and subsequent calcium oxalate stone formation. In addition, magnesium directly inhibits crystallization of stone-forming calcium salts, and therefore low urinary magnesium leads to reduced inhibitory activity. Low magnesium levels occur with poor dietary intake<sup>43</sup> or as a result of reduced intestinal absorption associated with intestinal abnormalities producing chronic diarrheal syndrome.<sup>32</sup>

### *Low urine pH*

At low urine pH ( $<5.5$ ), the undissociated form of uric acid predominates, leading to uric acid or calcium stone formation. Calcium oxalate stones form as a result of heterologous nucleation with uric acid crystals. Although any disorder leading to low urine pH may predispose to stone formation, 'gouty diathesis' refers to a stone-forming propensity

characterized by low urine pH of unclear etiology with or without associated gouty arthritis.<sup>44</sup>

### *Cystinuria*

Cystinuria is an autosomal recessive disorder characterized by a defect in intestinal and renal tubular transport of dibasic amino acids, resulting in excessive urinary excretion of cystine.<sup>45,46</sup> Cystine is poorly soluble in urine, and therefore precipitation of cystine and subsequent stone formation occur under physiologic urine conditions.<sup>9</sup>

### *Infection stones*

Struvite (magnesium ammonium phosphate) stones occur only in association with urinary infection by urea-splitting bacteria.<sup>47</sup> Under these conditions, urinary urea is hydrolyzed to ammonia by bacterial urease, resulting in alkaline urine that further promotes phosphate dissociation and allows formation of magnesium ammonium phosphate stones. Calcium phosphate stones are commonly found in association with struvite stones due to the favorable conditions of high urine pH that accompany struvite stone formation.

## **Medical evaluation**

In order to identify the underlying metabolic derangements responsible for stone formation, a careful medical and dietary history should be taken and blood and urine samples obtained for biochemical analysis. However, the extent of the evaluation and the need for medical vs dietary therapy will depend on the individual patient and the likelihood of recurrent stone formation.

### *Patient history*

The first step in the medical evaluation of stone disease is a careful medical and dietary history aimed at identifying medical or environmental conditions that predispose to nephrolithiasis. Systemic illnesses that may be associated with stone disease include intestinal disorders associated with chronic diarrhea (inflammatory bowel disease or bowel resection), sarcoidosis, hyperthyroidism, distal RTA, gout, immobility, malignancy, and bone disease. In addition, states of dehydration associated with vigorous exercise, or excessive dietary intake of dairy, animal protein, or salt may predispose to stone formation.

Several medications have been associated with nephrolithiasis either directly or indirectly. Ephedrine,<sup>48,49</sup> triamterene,<sup>50</sup> guaifenesin,<sup>49</sup> silicate,<sup>51</sup> and indinavir<sup>52,53</sup> have all been associated with stones composed of the drug itself in patients who consumed excessive amounts. Other medications indirectly promote stone formation by increasing urinary stone risk factors. Corticosteroids, vitamin D, and phosphate-binding antacids can induce hypercalciuria. Thiazides cause intracellular acidosis and subsequent hypocitraturia.<sup>33</sup> Acetazolamide, a carbonic anhydrase inhibitor, leads to urinary

alkalinization and hypocitraturia.<sup>54</sup> Lastly, cytotoxic agents promote a high cell turnover that results in urinary excretion of large amounts of uric acid.

### *Diagnostic tests*

Minimum baseline studies should include a urinalysis and culture; a plain radiograph of the kidneys, ureters, and bladder; a stone analysis; and serologic measurement of calcium, phosphorus, potassium, bicarbonate, uric acid, and creatinine.<sup>55</sup> Some findings establish a diagnosis without the need for corroborating evidence, such as cystine crystals on urinalysis or a urine culture positive for urea-splitting bacteria. Other factors may not be diagnostic but can suggest a pathophysiologic etiology. Low urine pH (<5.5) may suggest gouty diathesis, while a high pH (>7.5) suggests infection with a urea-splitting organism. Radiographic imaging studies may distinguish radiopaque stones (calcium oxalate, calcium phosphate, struvite, cystine) from radiolucent stones such as uric acid.

Knowledge of the stone composition may establish a diagnosis of stone etiology or help direct further evaluation. Stone analysis is generally performed by X-ray crystallography<sup>56</sup> or infrared spectrophotometry,<sup>57,58</sup> although a new technique of coherent scatter analysis using diagnostic X-rays has potential as a tool for determination of urinary calculus composition in vivo.<sup>59</sup> The finding of struvite or cystine stones is diagnostic for the underlying pathology. Likewise, uric acid stones imply acid urine. Serologic findings may also suggest a cause for stone disease. Primary hyperparathyroidism is associated with an elevated serum calcium, low serum phosphorus, and inappropriately high intact PTH level. RTA is characterized by low serum bicarbonate, hypokalemia, and hyperchloremia.

Urine collected over a 24-hour period is evaluated for urine biochemistry to identify metabolic, environmental, or physicochemical abnormalities that result in stone formation.<sup>55</sup> Metabolic risk factors include hypercalciuria, hyperoxaluria, hypocitraturia, high or low urine pH, and hyperuricosuria. Environmental risk factors include low total urine volume, elevated urinary sodium, hypomagnesiuria, and high urine sulfate. Physicochemical risk factors include increased relative supersaturation of calcium oxalate, calcium phosphate, uric acid, and monosodium urate.<sup>55</sup>

### *Individualization of metabolic evaluation*

The extent of the evaluation, whether detailed or simple, depends on the individual circumstances of each patient. Patients who present after their first stone episode and have no additional risk factors (i.e. no family history of stones, bone or bowel disease, or gout or chronic urinary tract infection) may require only a careful history and physical examination with minimal diagnostic tests. These patients may be adequately served by general, conservative dietary recommendations.<sup>60</sup> However, the recommendation of a limited evaluation in low-risk, first-time stone formers is not meant to imply that these patients are without metabolic and environmental risks. Yagisawa and associates identified 1.46 abnormalities per patient in firsttime stone formers, with low urine volume and absorptive hypercalciuria being the most common abnormalities.<sup>61</sup> Likewise, Pak identified metabolic abnormalities in nearly 80% of patients with a history of only a single stone episode. Although the first-time stone formers were found to have urinary

biochemical or serum abnormalities comparable to those of patients who are recurrent stone formers,<sup>62</sup> this select group of patients may be candidates for a trial of conservative dietary measures rather than drug therapy.

Although the need for evaluation of patients with recurrent stones or those who are at high risk of recurrent stone formation is generally accepted, the extent of the optimum evaluation is controversial. With an extensive evaluation, most recurrent stone formers are found to have at least a single metabolic abnormality, and over half have more than one abnormality.<sup>44</sup> Yagisawa and colleagues compared diagnostic information from limited (one or two, 24-hour urine collections) and comprehensive (two random 24-hour urine collections, one 24-hour urine collection after a week of dietary restriction, and a calcium load test) metabolic evaluations in recurrent calcium stone formers and found that the comprehensive metabolic evaluation yielded a specific metabolic abnormality in 90% of patients compared with 68% for a single urine collection and 75% for two 24-hour urine collections.<sup>63</sup> The average total number of specific metabolic abnormalities per patient was approximately 50% higher when based on a comprehensive metabolic evaluation (multiple collection) than when based on a single 24-hour urine collection ( $1.59 \pm 0.08$  SD vs  $0.94 \pm 0.07$  SD,  $p < 0.05$ ). Hypercalciuria, hyperoxaluria, and hypocitraturia were diagnosed significantly more often by the comprehensive than by the limited evaluation.

Bek-Jensen and Tiselius tested the reliability of one vs several urine collections in their clinical evaluation and found marked intra-individual variation in all parameters.<sup>64</sup> However, in more than 80% of cases, two 24-hour urine samples were sufficient to establish whether the patient had a normal or an abnormal urine composition. In contrast, Pak and coworkers compared 2 random 24-hour urine samples and found a highly significant positive correlation in risk factors between the samples, and thus determined that a single stone-risk analysis is sufficient for a simplified metabolic evaluation.<sup>65</sup>

A variety of different approaches, from simplified to extensive evaluations, have been described.<sup>16,44,55,66,67</sup> For a simplified evaluation, a single 24-hour urine is collected while the patient consumes an unrestricted diet. The 24-hour urine is analyzed for metabolic factors (calcium, oxalate, uric acid, citrate, pH), environmental factors (total volume, sodium, sulfate, phosphorus, magnesium), and physiochemical factors (urinary saturation of calcium oxalate, brushite, monosodium urate, uric acid). Subsequently, short-term (1 week) dietary modification is imposed, including increased fluid intake, based on the results of the first 24-hour urine collection. A repeat 24-hour urine sample is then collected to verify a reduction in environmental risk factors.

A more extensive evaluation involves collection of two 24-hour urine specimens obtained with the patient on a random diet. The patient is then instructed to observe a diet restricted in calcium (400 mg daily) and sodium (100 mEq daily) with avoidance of oxalate-rich foods. A third 24-hour urine specimen is collected after 1 week of restricted diet, after which a fast and load calcium test is performed to differentiate the subtypes of hypercalciuria. This test involves collecting a 2-hour fasting urine specimen that is analyzed for calcium, creatinine, pH, and total volume, after which a 1 g calcium load is administered orally, followed by collection of a 4-hour urine specimen that is analyzed for calcium, creatinine, and total volume. Urinary calcium exceeding 200 mg/day on a restricted diet defines hypercalciuria. Fasting hypercalciuria (urinary calcium/creatinine ratio of 0.11 or greater) with normal serum calcium suggests impairment in renal

reabsorption (renal hypercalciuria) but may also be seen in severe forms of absorptive hypercalciuria. Absorptive hypercalciuria is defined by a calcium/creatinine ratio of 0.22 or greater after ingestion of a 1 g calcium load. The fast and load calcium test is reliable only after 1 week of sodium and calcium restriction.

For most patients with recurrent stones, a 'simplified' approach is more practical and cost-effective than an extensive evaluation. The additional differentiation of causes of hypercalciuria does not change most treatment regimens and adds to the complexity and cost of evaluation. However, an individualized approach to each patient will help maximize diagnostic information and optimize therapy.

### **Medical management strategies**

The primary goal after initial management of an acute stone event is to reduce the rate of stone recurrence with a long-term management strategy. Approximately 50% of first-time stone formers have a recurrence within 5 years of diagnosis of their first stone if they receive no medical treatment.<sup>68,69</sup> The prognosis for recurrent stone formers is even worse, with as many as one or more stones developing per year.<sup>70-72</sup> Several different treatment strategies can be implemented to reduce the rate of stone recurrence. The simplest and least expensive involves dietary modification and increased fluid intake. This strategy avoids an extensive metabolic evaluation but may lead to higher stone recurrence rates in patients with metabolic abnormalities that cannot be corrected by conservative dietary measures alone. Alternatively, all patients can be treated empirically with medication aimed at stone prevention. Currently, the literature does not provide sufficient evidence to promote selective (medication aimed at correcting underlying metabolic abnormalities) vs nonselective medical therapy.<sup>73</sup> However, while identification and treatment of specific metabolic defects may not in the long run be necessary, empiric therapy has the disadvantages of increased cost, unnecessary treatment of patients without metabolic abnormalities, and the associated sideeffects that may result from medication. A third approach is treatment of patients with selective medical therapy based on a simplified or comprehensive metabolic evaluation. This strategy has the disadvantage of the added cost and minor inconvenience of the metabolic evaluation itself, but it has the advantage of treating patients with medication only when they demonstrate specific abnormalities that require drug therapy.

### *Dietary modification*

Dietary factors have long been known to influence the urinary environment and modulate the risk of stone formation. Indeed, dietary modification can reduce stone formation and in certain cases eliminate the need for medication. This 'stone clinic' effect has been shown to significantly reduce stone recurrence.<sup>60,74</sup> Hosking and colleagues found no stone growth or new stone formation (metabolic inactivity) in 63 of 108 patients (58%) treated with dietary modification alone, including 12 of 17 (71%) with hypercalciuria and 7 of 15 (47%) with hyperuricosuria, after a mean follow-up of 63 months.<sup>60</sup> Iguchi and colleagues found that dietary measures not only reduced stone recurrence rates compared with rates in controls but also lowered the rate of stone recurrence in patients additionally

treated with medication.<sup>74</sup> Indeed, a 52–86% reduction in stone recurrence rates compared with predicted rates was detected with dietary measures alone in the control arms of several drug treatment studies.<sup>18,75–78</sup>

Several dietary factors have been found to influence stone formation, including fluid intake, salt, calcium, oxalate, and animal protein. Kocvara and associates performed a multicenter, prospective, randomized trial comparing the effectiveness of specific dietary measures based on comprehensive metabolic evaluation and close follow-up (group 1) with nonspecific dietary recommendations and limited follow-up (group 2) in first-time calcium stone formers.<sup>79</sup> Stones recurred in 6% of the 113 patients in group 1 compared with 19% of the 94 in group 2 ( $p<0.01$ ), suggesting that specific dietary therapy, initiated and adjusted according to a metabolic evaluation, is more effective than nonspecific dietary recommendations in preventing the subsequent formation of stones.

### Fluids

A high fluid intake is the oldest existing treatment for kidney stones and arguably the most cost-effective. The benefit of fluids in reducing the risk of nephrolithiasis is derived from the dilution of stone-forming constituents and the subsequent reduction in urinary relative supersaturation,<sup>80</sup> while not affecting the inherent activity of natural inhibitors.<sup>81</sup> Several retrospective studies have confirmed the benefit of high fluid intake in reducing risk of stone recurrence.<sup>60</sup> Hosking and colleagues followed a group of 108 recurrent stone formers and found that 24-hour urine volumes were higher in patients who were metabolically inactive (2136 ml) compared with those who had recurrent stone episodes (1726 ml) ( $p<0.005$ ).<sup>60</sup> Strauss et al also found that among patients with recurrent idiopathic calcium nephrolithiasis those who relapsed ( $n=57$ ) decreased their urine volume during treatment while those who remained stone free for at least 2 years ( $n=189$ ) increased their urine volume during the study period.<sup>20</sup>

The relationship between fluid intake and kidney stones was prospectively studied over 4 and 12 years, respectively, in a cohort of 45,289 male health-care professionals<sup>82</sup> and 81,093 female nurses<sup>83</sup> who had no previous history of kidney stones. In both studies, fluid intake was inversely related to the risk of stone formation. Comparing the highest quintile of fluid intake to the lowest yielded a relative risk of stone formation of 0.71 (95% CI 0.52–0.97) in the male cohort and 0.61 (95% CI 0.48–0.78) in the female cohort.

The value of a high fluid intake has also been validated in two prospective studies. Frank and De Vries instructed recent immigrants to a small Israeli town with a high propensity for stone formation on the benefits of a high fluid intake.<sup>84</sup> Over a 3-year period, the instructed group demonstrated a higher urine output and decreased number of stone events compared with the long-term residents. Borghi and colleagues randomized 199 first-time stone-formers to either a group with high fluid intake, enough to produce at least 2 liters of urine daily ( $n=99$ ), or a group that received no recommendations ( $n=100$ ).<sup>85</sup> After 5 years, the high-fluid group was noted to have a higher urine volume and fewer stone recurrences (12%) than did the control group (27%) ( $p=0.008$ ). Furthermore, the mean time to recurrence was longer in the high-fluid group than in the control group (39 months vs 25 months, respectively).

The relative benefit of specific beverages other than water has not been well studied. In the large observational studies of Curhan and colleagues the risk of incident stone

formation decreased by 10%, 14%, 21%, and 39% for coffee, tea, beer, and wine, respectively, in the male cohort, and by 10%, 8%, and 59% for coffee, tea, and wine, respectively, in the female cohort. On the other hand, the risk of stone formation increased by 37% and 44% for grapefruit juice in the two studies.<sup>82,83</sup>

The finding of an increased risk of stone formation with grapefruit juice in the cohort studies of Curhan conflicts with the findings of several metabolic studies that show no effect of grapefruit juice<sup>86</sup> and a beneficial effect of other citrus juices such as orange juice<sup>87</sup> and lemonade.<sup>88</sup>

### Protein

Animal protein has long been recognized as a risk factor for calcium stone disease.<sup>89</sup> Stone formers have been found to consume more animal protein than normal subjects.<sup>90</sup> In addition, both male and female hypercalciuric stone formers have been noted to have a higher protein and sodium intake than normocalciuric stone formers and, when matched for urea excretion, their mean urinary calcium excretion is higher.<sup>91</sup>

Animal protein excess is thought to increase stone risk by increasing urinary uric acid due to purine excess and by inducing hypocitraturia and hypercalciuria by providing an acid load. A low animal protein intake is associated with a reduced excretion of calcium, oxalate, and uric acid and, consequently, a low relative probability of forming stones.<sup>89</sup> On the other hand, a high protein diet has been associated with elevated urinary calcium, uric acid, and sulfate and a decreased urinary citrate level, all of which increase stone propensity.<sup>92</sup> Animal protein intake was directly associated with the risk of incident stone formation in the cohort studies of Curhan and colleagues (relative risk 1.33, 95% CI 1.00–1.77).<sup>90</sup>

Rotily and associates evaluated the impact of a low protein or high fiber diet on urinary risk factors in 96 idiopathic calcium stone formers who were randomly assigned to a low animal protein diet (<10% of total energy), a high fiber diet (>25 g/day), or a random diet (control group); all patients were encouraged to increase their fluid intake.<sup>93</sup> At 4 months, 12 out of 31 patients assigned to a low animal protein diet achieved a reduction in urine urea excretion of more than 50 mmol/day and also exhibited a significant decrease in urinary calcium excretion, averaging 1.8 mmol/day. A significant correlation between urea and calcium excretion was observed only among patients with hypercalciuria. Several other investigators have noted a similar improvement in stone risk factors for hypercalciuric stone formers on protein-restricted diets.<sup>94,95</sup>

Breslau and colleagues evaluated 15 normal subjects in a three-way randomized crossover study involving three 12-day phases of study in which subjects were maintained on a controlled metabolic diet containing vegetable protein, vegetable and egg protein, or animal protein, with increasing sulfate content in the 3 diets.<sup>34</sup> As the fixed acid content of the diets increased, urinary calcium excretion increased from 103 mg/day on the vegetarian diet to 150 mg/day on the animal protein diet ( $p<0.02$ ). Moreover, the animal protein-rich diet was associated with the highest excretion of undissociated uric acid and lowest citrate excretion due to the reduction in urinary pH. Urinary crystallization studies revealed that the animal protein diet, when electrolyte composition and quantity of protein were kept the same as for the vegetarian diet, conferred an

increased risk for uric acid stones, but because of opposing factors, not for calcium oxalate or calcium phosphate stones.

Despite the favorable improvement in urinary risk factors associated with dietary animal protein restriction, Hiatt et al failed to observe a beneficial effect of a low protein diet in a prospective, randomized trial of 102 calcium oxalate stone formers assigned either to a low animal protein (56–64 g daily); a high fiber, high fluid diet; or to a regimen of high fluid intake only.<sup>96</sup> At a mean follow-up of 3.4 years, 24% of the subjects in the low protein group and only 4% of the control subjects developed a new stone (relative risk 5.6, 95% CI 1.2–26.1). Of note, however, the control group had a higher mean urine volume than the intervention group at two of the three follow-up visits, which could have confounded the results.

### Sodium

High sodium intake has been associated with an increased risk of stone formation because of its propensity to increase urinary calcium and pH and to reduce urinary citrate.<sup>97,98</sup> Stone formers may in fact be more sensitive than normal subjects to the calciuric effects of protein and sodium.<sup>99</sup> In the two large observational studies by Curhan and colleagues a high salt intake was associated with an increased risk of incident stone-formation in women (relative risk 1.30, 95% CI 1.05–1.62, comparing highest quintile to lowest quintile of sodium intake) but not in men.<sup>90,100</sup> In addition, Borghi et al found that a diet with normal calcium intake (30 mmol/day), but limited animal protein (52 g/day) and salt (50 mmol/day), was more effective in reducing stone recurrence than a low calcium diet, although sodium was not an independently controlled variable.<sup>101</sup>

### Calcium

The role of dietary calcium in stone formation is controversial.<sup>73,102</sup> Although dietary or supplemental calcium intake correlates with urinary calcium, hypercalciuria has never been directly linked with calcium stone formation. Nonetheless, dietary calcium restriction has been commonly recommended in calcium stone formers to prevent stone recurrence. Recently, this practice has been called into question, because of the risk of bone loss and the uncertainty regarding its utility. Indeed, the two large cohort studies by Curhan and colleagues found a protective effect of high calcium intake on the risk of stone formation.<sup>90,100</sup> When the highest quintile of dietary calcium intake (mean 1326 mg/day in men and 1119 mg/day in women) was compared with the lowest (mean 516 mg/day in men and 430 mg/day in women), the relative risk of stone formation was 0.66 (95% CI 0.49–0.90) and 0.65 (95% CI 0.50–0.83) for the male and female cohorts, respectively. The protective effect of dietary calcium intake against stone formation was attributed to intestinal binding of oxalate by calcium, which reduced oxalate absorption and subsequent urinary oxalate excretion.

Interestingly, the relative risk in women who took supplemental calcium compared with that in women who did not was 1.20 (CI, 1.02–1.41).<sup>83</sup> Of note, 67% of women who took supplemental calcium consumed the calcium with breakfast or apart from a meal. Thus, the authors speculated that the protective effect of calcium-binding oxalate in the intestine is lost when the calcium is consumed at times of low oxalate intake.



Several authors, however, have questioned the interpretation of these studies.<sup>73,102,103</sup> Several confounding factors, including higher intake of fluid, potassium, magnesium, and phosphate in the group comprising the highest quartile of calcium intake, were not fully accounted for in these cohort studies. Furthermore, oxalate and alkali intake were not assessed.<sup>73</sup> Heller et al, in fact, performed a two-phase, randomized, crossover study of 21 normal subjects in which the diets from the highest and lowest quintile of calcium intake were duplicated in a controlled metabolic diet. Not surprisingly, urinary calcium was significantly higher in patients on the high calcium as opposed to the low calcium diet (148 vs 118 mg/day,  $p < 0.01$ ). However, urinary oxalate did not differ significantly between the two diets. Because of the other differences in the two diets (more fluid, potassium, magnesium, and phosphate in the high calcium group), there was no difference in the relative saturation ratio of calcium oxalate between the two diets. After adjustments were made for these confounding variables, however, the high calcium diet was found to raise the relative saturation ratio of calcium oxalate by 24% ( $p = 0.03$ ). The proposed increase in urinary oxalate that was theorized to account for the greater stone risk in the low calcium group was not validated by this study, probably because of the modest oxalate intake by patients on the controlled metabolic diet that provided insufficient oxalate for absorption after calcium oxalate binding. This study suggests that a high calcium diet, in the absence of additional protective dietary measures, may pose a risk for stone formation.<sup>104</sup>

Furthermore, a recent re-evaluation of the subjects from the cohort studies by Curhan and associates found no significant difference in urinary oxalate between the subjects who formed stones and those who did not.<sup>105</sup> Indeed, hypercalciuria among the urinary risk factors carried the highest risk of stone formation.

In the only prospective, randomized trial to date that assesses the effect of calcium intake on stone risk, Borghi and colleagues randomized 120 hypercalciuric males who had recurrent calcium oxalate stones to a normal calcium, low sodium, low protein diet or a low calcium diet.<sup>101</sup> After 5 years, the low calcium group experienced a statistically higher rate of stone formation than the normal calcium group (38% vs 20%, respectively, relative risk=0.49). Although urinary calcium decreased by a comparable degree in both groups, urinary oxalate decreased in the normal calcium group (78 mmol/day) but increased in the low calcium group (44 mmol/day), thereby presumably accounting for the increased rate of stone recurrence in the low calcium group.

Further studies are necessary to fully elucidate the effect of dietary calcium on stone risk and the role of intestinal calcium oxalate interaction on urinary stone risk factors. At this time, severe calcium restriction should be discouraged, and calcium intake in hypercalciuric stone formers should be guided by urinary calcium and bone mineral density.

## Oxalate

Urinary oxalate levels impact calcium oxalate supersaturation and subsequent stone formation. The relative contribution of dietary oxalate versus in-vivo metabolism on urinary oxalate excretion is controversial but has recently been addressed by Holmes and colleagues, who measured urinary oxalate levels in subjects consuming diets containing variable, known amounts of oxalate.<sup>106</sup> Urinary oxalate excretion increased with dietary

oxalate intake and the contribution of dietary oxalate to urinary oxalate varied from 24% to 53%, depending on dietary oxalate and calcium content. Hess and associates found that increased calcium intake during liberal oxalate intake prevented hyperoxaluria, confirming the importance of intestinal calcium oxalate interaction.<sup>107</sup> Therefore, restriction of foods associated with a high oxalate content, such as chocolate, cocoa, brewed tea, nuts, beets, spinach, rhubarb, chives, and brown rice, is recommended, particularly in patients with known hyperoxaluria.

Ascorbic acid (vitamin C) has been implicated as a risk factor for calcium oxalate stone formation based on in-vivo conversion to oxalate and its potential to lower urinary pH.<sup>73</sup> Studies evaluating the effect of large doses of ascorbic acid on urinary oxalate have yielded contradictory results, in part because of inaccuracy in measuring urinary oxalate in the presence of ascorbate, which may be readily oxidized in vitro to oxalate. In a recent two-phase, randomized, double-blind crossover study involving 12 normal subjects and 12 calcium oxalate stone formers administered 2 g of ascorbic acid or placebo while maintained on a controlled metabolic diet, Traxer and colleagues found no difference in urine pH between the two phases for either the normal subjects or stone formers, but in both groups urinary oxalate increased significantly in the ascorbic acid phase compared with the placebo phase.<sup>108</sup> Based on these findings, the authors recommended limiting ascorbic acid consumption to less than 2 g daily.

Despite the observations of these investigators and others, there is little clinical evidence linking ascorbic acid intake with increased stone occurrence. Indeed, Curhan's cohort study found no association between ascorbic acid intake and stone formation in men or women.<sup>39,40</sup>

### *Drug treatment*

For patients in whom conservative therapy fails or for those patients with active stone disease in whom metabolic derangements have been identified, conservative dietary measures should be accompanied by medical therapy targeted at correcting the underlying metabolic disturbances that lead to stone recurrence. Because medication use involves both cost and inconvenience to patients, the decision to initiate drug therapy should be individualized to each patient. For those patients who present after their initial stone episode and have a low likelihood of stone recurrence, the decision may be to begin with dietary modification prior to proceeding with medication.

The issue of noncompliance is an important consideration when initiating drug treatment. Numerous studies have noted noncompliance rates of up to 30%.<sup>70,71,76</sup> Although this problem is not unique to stone patients, it is a major concern considering the high lifelong risk of recurrence. The reasons for noncompliance include not only side-effects of medications but also loss of interest. When Ettinger and colleagues prospectively randomized recurrent stone formers to placebo, magnesium hydroxide, and hydrochlorothiazide treatment arms, loss of interest resulted in drop-out rates of 14%, 18%, and 18% for the three arms, respectively, while adverse drug reactions resulted in drop-out rates of 4%, 13%, and 21%, respectively.<sup>76</sup> Therefore, the importance of emphasizing to patients the lifelong risk of stone formation and the need for adherence to recommendations regarding diet and medication cannot be overemphasized.

Numerous studies have evaluated the effectiveness of drug therapy in reducing stone recurrence. Unfortunately, surprisingly few randomized, placebo-controlled trials have been performed, and most studies compared active treatment groups with historical controls rather than placebo groups or nontreatment control groups. Furthermore, many trials evaluated the efficacy of drug treatment in correcting urinary biochemical parameters rather than stone recurrence, assuming these intermediary parameters serve as a proxy for stone recurrence. Unfortunately, the validity of such links between urinary biochemical parameters, such as urinary calcium, and the outcome parameter, stone recurrence, has never been established. As such, the only reliable measure of drug efficacy is to measure stone recurrence. Because of the relative infrequency of the event (stone recurrence), long periods of observation are required, thereby necessitating long-term clinical trials.

Pearle and colleagues performed a meta-analysis of randomized trials in the literature to determine the efficacy of commonly used medications compared with placebo or no treatment for the prevention of stone recurrence.<sup>109</sup> A literature search identified 14 randomized, controlled trials comprising 20 treatment arms and six different drug therapies for the prevention of stone recurrence. A statistically significant benefit of drug therapy for stone metaphylaxis was identified ( $p=0.04$ ), largely because of the benefit of thiazides compared with placebo or no treatment ( $p=0.02$ ). Allopurinol conferred no overall benefit, although the only trial evaluating therapy selectively in hyperuricosuric patients showed a statistically significant benefit. There were insufficient trials for adequate assessment of the effectiveness of alkali citrate.

### Selective medical therapy

The identification of specific pathophysiologic abnormalities associated with particular forms of stone disease enables the initiation of selective medical regimens aimed to correct the underlying disorders. Table 26.1 summarizes specific treatment recommendations based on the associated metabolic derangement.

**Hypercalciuria.** Because the mechanism responsible for intestinal hyperabsorption of calcium is unknown, treatment of AH is empiric and aimed at reducing urinary calcium excretion. Thiazide diuretics constitute first-line therapy for AH Type I although they have no effect on intestinal calcium absorption. However, they counteract hypercalciuria by acting on the distal renal tubule to inhibit sodium reabsorption and enhance calcium reabsorption.<sup>108</sup> In addition, by inducing volume depletion they indirectly lead to enhanced sodium and calcium reabsorption in the proximal tubule, further reducing urinary calcium. The hypocalciuric action of thiazides may be limited in patients with absorptive hypercalciuria to a period of 18–24 months.<sup>110</sup> In this case, a brief drug holiday, with cessation of the drug or substitution of another medication may restore effectiveness after a period of approximately 6 months.

The recommended doses of commonly used thiazide diuretics for a normal-sized adult are trichloromethiazide 2–4 mg daily, hydrochlorothiazide 25–50 mg daily, and bendroflumethiazide 2.5 mg twice daily. An alternative, nonthiazide diuretic, indapamide (1.25–2.5 mg daily) has a similar mechanism of action to the thiazides. Thiazides have been used both selectively and nonselectively in patients with idiopathic calcium stones and in patients with hypercalciuria. Thiazide use may be limited by sideeffects, including

fatigue, impotence, light-headedness, musculoskeletal symptoms, and gastrointestinal complaints, in 30–50% of patients.<sup>19,76</sup> In addition, thiazide-induced hypokalemia, hyperuricosuria, metabolic alkalosis, and rarely liver dysfunction may occur. Indeed, thiazide-induced hypokalemia may promote intracellular acidosis and subsequent hypocitraturia. In order to prevent thiazide-induced hypokalemia and hypocitraturia, the addition of potassium citrate (10–20 mEq twice daily) has been shown to reduce stone recurrence in hypocitraturic patients unresponsive to thiazide therapy despite an adequate hypocalciuric response.<sup>110</sup>

Orthophosphate, the neutral salt of phosphorus, has been advocated by some investigators to correct hypercalciuria, particularly when it is associated with renal phosphate leak, a hypophosphatemic variant of AH. Orthophosphate restores serum phosphate levels, thereby lowering circulating levels of 1,25-(OH)<sub>2</sub> vitamin D and decreasing intestinal calcium absorption, ultimately

**Table 26.1** *Pathogenetic factors and corresponding treatment*

| Condition                               | Metabolic/environmental defect   | Treatment                             | Physiologic action   |
|---|--|---------------------------------------|--|
| Hypercalciuria                          |  |                                       |  |
|   | ↑ GI calcium absorption  | Thiazides                             | ↓ urinary calcium (12–18 months)<br>↓ urinary citrate  |
| Absorptive                              |  | Potassium citrate                     | ↑ urinary citrate<br>↓ urinary calcium   |
| Renal                                   | Impaired renal calcium reabsorption  | Thiazides                             | ↓ urinary calcium (sustained effect)<br>↓ urinary citrate<br>↓ intestinal calcium absorption (by ↓ 1,25-(OH) <sub>2</sub> vitamin D) |
|   |  | Potassium citrate                     | ↑ urinary citrate<br>↓ urinary calcium   |
| Resorptive                              | Primary hyperparathyroidism  | Parathyroidectomy                     | Normalizes serum PTH and calcium   |
| Hyperuricosuric calcium nephrolithiasis | Dietary purine excess, uric acid overproduction, increased renal uric acid excretion | Allopurinol                           | ↓ urinary uric acid  |
|   |  | Potassium citrate                     | ↑ urinary citrate  |
| Hypocitraturic calcium nephrolithiasis  |  |                                       |  |
| Isolated                                | Idiopathic   |                                       |  |
| Chronic diarrhea                        | GI alkali loss Hypokalemia   | Alkali citrate                        | ↑ urinary citrate  |
| Thiazide-induced RTA                    | Impaired renal acid excretion  |                                       |  |
| Hyperoxaluric calcium nephrolithiasis   |  |                                       |  |
| Primary                                 | Oxalate overproduction   | Low oxalate diet<br>Pyridoxine Liver- | ↓ urinary oxalate<br>↓ urinary oxalate   |

|                  |  |  |                               |
|------------------|--|--|-------------------------------|
|                  |  | kidney transport                               | Normalizes oxalate metabolism |
| Dietary          | ↑ dietary oxalate                        | Low oxalate diet                               | ↓ urinary oxalate             |
| Enteric          | ↑ intestinal oxalate absorption          | Potassium citrate                              | ↓ urinary oxalate             |
|                  |  | Calcium citrate                                | ↑ urinary citrate             |
|                  |  |  | ↓ urinary citrate             |
|                  |  |  | ↓ urinary oxalate             |
| Gouty diathesis  | Low urinary pH                           | Potassium citrate                              | ↑ urinary pH                  |
|                  |  |  | ↑ urinary citrate             |
| Cystinuria       | Impaired renal cystine reabsorption      | D-penicillamine or α mercaptopropionyl glycine | disulfide bond with cysteine) |
| Infection stones | Infection with urease-producing bacteria | Acetohydroxamic acid                           | Inhibits urease               |
|                  |  |  | ↑ urine pH                    |
|                  |  |  | ↓ urinary ammonium            |

↑=increased; ↓=decreased; GI=gastrointestinal; PTH=parathyroid hormone. RTA=renal tubular acidosis.

lowering urinary calcium.<sup>111</sup> Although orthophosphate additionally raises the concentration of urinary inhibitors, including pyrophosphate and citrate, it also increases urinary saturation of calcium phosphate.<sup>113</sup> Despite the beneficial effect of orthophosphate on urinary stone risk factors, however, none of the three placebo-controlled randomized trials demonstrated a reduction in stone recurrence in recurrent calcium stone formers treated with a variety of orthophosphate preparations.<sup>42,72,114</sup>

Orthophosphate is available as a mixture of neutral salts of sodium and potassium phosphate, as alkaline phosphate, or as acid potassium phosphate. The recommended dosage is 1–2 g daily in 3–4 divided doses. The most common sideeffect associated with phosphate preparations is diarrhea, which often resolves within a few weeks of therapy.

Renal hypercalciuria is optimally managed with thiazides as first-line therapy. Renal leak of calcium is overcome by thiazide-induced renal tubular calcium reabsorption. With normalization of serum calcium, serum PTH secretion is suppressed, thereby restoring serum 1,25-(OH)<sub>2</sub> vitamin D and normalizing intestinal calcium absorption. In contrast to the limited hypocalciuric response to thiazides observed in AH, which may be attenuated after 18–24 months, the hypocalciuric response is maintained in renal hypercalciuria.

AH Type II is correctable with modest dietary calcium restriction alone (400–600 mg calcium daily). However, in AH Type II patients with associated bone loss, the initiation of thiazide and potassium citrate may obviate the need for strict calcium restriction and prevent further bone loss. Indeed, Pak and colleagues showed that with moderate calcium and oxalate restriction, along with a thiazide or indapamide plus potassium citrate, L2–4 vertebral bone mineral density increased by 5.7% and stone formation decreased significantly after a mean of 3.7 years of treatment.<sup>104</sup>

A total of eight prospective, randomized trials have evaluated the efficacy of thiazide diuretics (one with indapamide, a nonthiazide diuretic with a similar mechanism of action), although the duration of therapy, type of drug, patient selection, and type of controls varied.<sup>18,19,72,75–78,114</sup> Table 26.2 summarizes the results of the trials and compares the outcomes of the control arms and the treatment arms. In two of the trials, the

medication was used selectively in hypercalciuric patients only<sup>18,75</sup> and in the remainder the medication was used in calcium stone formers regardless of metabolic background. Despite variations in trial design, six of the eight trials demonstrated a significant benefit of treatment over placebo or dietary modification.<sup>18,72,75–77,114</sup> The two trials that failed to show a significant benefit of medication had less than 1.5 years of follow-up, which may not be long enough to establish a difference.<sup>19,78</sup> Overall, the treatment arms demonstrated a post-treatment stone rate of 0.13 stones/patient/year compared with 0.3 stones/patient/year in the placebo arms, representing a 57% risk reduction.

Resorptive hypercalciuria associated with primary hyperparathyroidism is treated with surgical removal of the abnormal parathyroid gland(s). Alternatively, for patients not considered surgical candidates, medical therapy may be offered for primary hyperparathyroidism. Broadus and associates treated 10 patients who had primary hyperparathyroidism with oral phosphate therapy for 12 months and observed a reduction in circulating levels of 1,25-(OH)<sub>2</sub> vitamin D and a decrease in serum calcium, although serum PTH increased even further above baseline.<sup>115</sup> Estrogen therapy has also been shown to result in a reduction in serum and urinary calcium and inhibition of PTH-induced bone resorption.<sup>115</sup>

**Hyperuricosuria.** For mild hyperuricosuria, dietary purine restriction may be sufficient to lower urinary uric acid excretion. Reducing intake of animal proteins, such as red meat, fish, and poultry, limits the substrate available for uric acid production and reduces urinary saturation of monosodium urate. In many cases, however, dietary restriction is inadequate to control uric acid excretion, and the initiation of drug therapy is necessary. Allopurinol (300 mg/day) is a xanthine oxidase inhibitor that prevents the conversion of hypoxanthine to xanthine and thereby reduces uric acid production and urinary excretion.<sup>73</sup>

Although four randomized trials have evaluated the efficacy of allopurinol compared with that of placebo/no treatment for the prevention of recurrent stones,<sup>72,114,117,118</sup> the only trial that demonstrated benefit of medication was the trial of Ettinger and colleagues in which hyperuricosuric patients were specifically selected for study.<sup>117</sup> Among 60 patients randomized to either allopurinol (100 mg three times daily) or placebo, the mean recurrence rate was 0.26 stones/patient/year in the placebo group compared with only 0.12 stones/patient/year in the allopurinol group.

Side-effects associated with allopurinol are few and are limited to skin rash and a reversible elevation of liver enzymes. The development of a skin rash should prompt immediate discontinuation of the drug because of reported progression to Stevens-Johnson syndrome.

For the rare patient who cannot tolerate allopurinol due to side-effects, and particularly for those with associated hypocitraturia, potassium citrate (30–60 mEq daily in divided doses) can serve as a substitute. Pak and Peterson noted a 75% reduction in the rate of stone formation in 19 patients with hyperuricosuric calcium oxalate nephrolithiasis treated with potassium citrate over a mean of 2.4 years.<sup>119</sup> Citrate, by complexing with calcium, reduces urinary saturation of calcium oxalate, and also directly inhibits monosodium urate-induced heterologous nucleation of calcium.<sup>120</sup>

**Hypocitraturia.** Potassium citrate delivers an alkali load that enhances urinary citrate excretion and increases renal

**Table 26.2** *Treatment with thiazide diuretics<sup>a</sup> vs placebo or no treatment in patients with recurrent calcium stones adapted with permission from Pearle et al<sup>109</sup>*

| Author                          | N   | F/U<br>(years) | Control      | Stones/pt/yr | N   | F/U<br>(years) | Treatment           | Stones/pt/yr | p-Value |
|---------------------------------|-----|----------------|--------------|--------------|-----|----------------|---------------------|--------------|---------|
| Borghiet al <sup>18</sup>       | 21  | 3              | Diet         | 0.28         | 19  | 3              | Indapamide          | 0.06         | < 0.05  |
| Ohkawa et al <sup>75</sup>      | 93  | 2.1            | Diet         | 0.31         | 82  | 2.2            | Trichlormethiazide  | 0.13         | < 0.05  |
| Ettinger et al <sup>76</sup>    | 31  | 3              | Placebo+diet | 0.22         | 23  | 3              | Chlorthalidone      | 0.05         | < 0.05  |
| Scholz et al <sup>19</sup>      | 26  | 1              | Placebo      | 0.23         | 25  | 1              | Hydrochlorothiazide | 0.24         | NS      |
| Laerum and Larson <sup>77</sup> | 25  | 3.2            | Placebo+diet | 0.15         | 23  | 3.3            | Hydrochlorothiazide | 0.07         | 0.05    |
| Brocks et al <sup>78</sup>      | 29  | 1.5            | Placebo      | 0.11         | 33  | 1.5            | Bendroflumethiazide | 0.09         | NS      |
| Wilson et al <sup>113</sup>     | 21  | 3              | No tx        | 0.31         | 23  | 3              | Hydrochlorothiazide | 0.15         | < 0.05  |
| Robertson et al <sup>72</sup>   | 93  |                | No tx        | 0.58         | 13  | 3              | Bendroflumethiazide | 0.22         | 'Sig'   |
| Weighted means                  | 255 | 2.3            | Control      | 0.27         | 241 | 2.3            | Thiazide            | 0.12         | —       |

<sup>a</sup> Included one trial using Indapamide, a nonthiazide diuretic with a similar mechanism of action to thiazides. N=number of patients; F/U=follow-up; pt/yr=patient/year; NS=not significant; tx=treatment; 'Sig'=significant.

calcium reabsorption.<sup>121</sup> The citraturic action of potassium citrate is largely accounted for by the alkali load, and potassium itself has little effect in the absence of potassium deficiency.<sup>122</sup> For patients who are unable to tolerate potassium citrate or in whom potassium-containing medications are contraindicated because of renal insufficiency, sodium citrate or sodium bicarbonate provides an alternative therapy. However, the additional sodium load may counteract the beneficial effects of enhanced citrate excretion by promoting urinary calcium excretion. Potassium citrate is administered at starting doses of 40–60 mEq daily in divided doses.

Although several retrospective studies have established the benefit of potassium citrate in reducing metabolic risk factors for stone formation and clinical recurrences,<sup>123–125</sup> only a few prospective randomized trials have compared alkali citrate to placebo.<sup>70,71,126</sup> Barcelo and associates prospectively randomized 57 patients with active stone disease (2 or more stones during the preceding 2 years) and idiopathic hypocitraturia to treatment with 45 mEq potassium citrate daily or placebo.<sup>70</sup> A significantly higher remission rate was seen with potassium citrate than with placebo (72% vs 20%, respectively), and a corresponding significant increase from baseline in urinary citrate, pH, and potassium was found in the treatment but not the placebo groups. Ettinger et al also prospectively

evaluated 64 patients with active, recurrent calcium stone disease and no secondary cause of nephrolithiasis who were randomly assigned to receive placebo or potassium magnesium citrate (42 mEq potassium, 21 mEq magnesium, and 63 mEq citrate) daily for up to 3 years.<sup>126</sup> New stones formed in 64% of patients in the placebo group compared with 13% of patients receiving potassium magnesium citrate. When compared with placebo, the relative risk of treatment failure for potassium magnesium citrate was 0.16 (95% CI 0.05–0.46). Interestingly, this study showed a benefit of potassium citrate therapy not only in hypocitraturic stone formers but also in nonselected calcium stone formers. Hofbauer and colleagues also assessed the efficacy of alkali citrate as a nonselective therapy in 50 patients with recurrent idiopathic calcium oxalate stone formation who were randomized to sodium potassium citrate or conservative treatment only.<sup>71</sup> Despite a statistically significantly higher urinary citrate excretion in the treated group, no difference was seen between the two groups with regard to recurrent stone formation. Likewise, Jendle-Bengtén and Tiselius found no long-term protection from recurrent calcium stone formation with a single evening dose of 3.75–5 g of sodium potassium citrate.<sup>127</sup> Of note, the use of sodium alkali citrate rather than potassium alkali citrate may have negated the beneficial effect of alkali therapy in these studies on the basis of sodium-induced hypercalciuria and increased monosodium urate.

In a novel use of potassium citrate, Soygur and associates randomized 90 patients with calcium stones 1 month after shock wave lithotripsy (SWL) for lower caliceal stones to treatment with oral potassium citrate (60 mEq daily) or no treatment.<sup>3</sup> Among 56 patients rendered stone free after SWL, the stone recurrence rate was 0% and 28.5%, respectively, for potassium citrate-treated vs control patients, respectively, after 12 months of follow-up. Among 34 patients with residual fragments, potassium citrate-treated patients showed resolution of their residual fragments in 44.5% compared with only 12.5% of control patients. Therefore, potassium citrate therapy improved stone clearance and recurrence rates in patients with and without stones after SWL treatment.

Potassium citrate has also been used for treatment of recurrent stone disease caused by distal RTA. Preminger et al examined the effect of 60–80 mEq daily of oral potassium citrate in 9 patients with incomplete distal RTA diagnosed on the basis of an abnormal response to an oral ammonium chloride load.<sup>31</sup> After 3 months of therapy, potassium citrate caused a significant increase in urinary pH and citrate and a decrease in urinary calcium from baseline. Moreover, during a mean treatment period of 34 months none of the 9 patients developed new stones.

**Hyperoxaluria.** Treatment of primary hyperoxaluria is aimed at reducing in-vivo oxalate production. Pyridoxine (vitamin B<sub>6</sub>) supplementation enhances the conversion of glyoxalate to glycine, thereby reducing the substrate available for conversion to oxalate. Dosages of 50–100 mg twice daily may be sufficient to reduce oxalate production and stone formation in these patients. Limited success has also been reported with magnesium supplementation<sup>128</sup> and a combination of orthophosphate and pyridoxine.<sup>129,130</sup> Since the liver is the only organ responsible for the detoxification of glyoxylate, combined liver-kidney transplant is accepted treatment for most patients with severe primary hyperoxaluria. Patient survival after transplant approximates 80% at 5 years and 70% at 10 years. In addition, the renal function of survivors reportedly remains stable over time.<sup>35</sup>



For patients with enteric hyperoxaluria, calcium supplementation may be beneficial because of its ability to bind intestinal oxalate and prevent excess oxalate absorption. These patients generally have markedly low urinary calcium levels because of poor intestinal absorption. However, although calcium supplementation rarely results in hypercalciuria, careful monitoring of urinary calcium is advisable in this setting. Calcium citrate offers the additional benefit of increasing urinary citrate and raising urinary inhibitory activity.<sup>131</sup>

Potassium citrate therapy is also of benefit in patients with enteric hyperoxaluria who have associated hypocitraturia and low urinary pH. Pyridoxine is of limited value in patients with enteric hyperoxaluria because most urinary oxalate derives from the diet rather than from metabolic pathways. However, dietary oxalate restriction and a trial of pyridoxine therapy is a simple, low-risk approach that may prove beneficial.

In all patients with hyperoxaluria, dietary restriction of oxalate-rich foods is essential. Furthermore, strict calcium restriction should be avoided to prevent excessive unopposed intestinal oxalate absorption.

**Hypomagnesuria.** Magnesium has been shown to increase urinary pH, citrate, and magnesium and therefore to decrease urinary saturation of calcium oxalate *in vitro*<sup>132</sup> and *in vivo*.<sup>105</sup> However, despite the beneficial effect of magnesium on urinary stone risk factors, two randomized trials comparing magnesium oxide with placebo or no treatment have failed to demonstrate benefit.<sup>76,32</sup>

**Low urine pH.** Low urine pH predisposes to the formation of both uric acid and calcium oxalate stones. Potassium citrate (40–60 mEq daily in 2–3 divided doses) raises urine pH and favors the dissociation of uric acid, thereby preventing uric acid and uric acid-induced calcium oxalate stone formation. Additionally, the increase in urinary citrate induced by the alkali load reduces calcium oxalate stone risk. The use of potassium rather than sodium alkali is preferred because the hypercalciuric action of sodium and the increase in monosodium urate may offset the beneficial effect of increased pH and citrate. Finally, restriction of animal protein intake is recommended because of the increased urinary acidity conferred by the high acid-ash content of animal protein.

**Cystinuria\*** Cystinuria is an inherited condition that affects the active transport of the dibasic amino acids cystine, ornithine, lysine, and arginine across the renal tubule and the small intestine. The only important clinical manifestation of the disorder is the production of cystine stones that form as a result of increased excretion of cystine, which is poorly soluble at normal urine pH. The goal of therapy is to reduce the concentration of cystine to a level below cystine solubility. The mainstay of treatment is high fluid intake (in excess of 1.5 l/m<sup>2</sup> per day), well distributed throughout the day and night, and urine alkalinization up to pH 7.0 by means of sodium bicarbonate and/or potassium citrate.<sup>9,12,45,46</sup> When these measures are ineffective in preventing stone occurrence, sulfhydryl agents such as D-penicillamine or  $\alpha$ -mercaptopropionyl glycine (Tiopronin), which form highly soluble mixed disulfides with cysteine moieties, should be added to the medical regimen, especially when cystine excretion exceeds 750 mg/day. Frequent clinical follow-up is needed to encourage patient compliance and assess efficacy and tolerance of treatment.<sup>9,45,46</sup> Tiopronin should be started at a dosage of 300–400 mg daily in divided dosages and titrated to effect up to 2400 mg daily. Urinary protein should be monitored closely because of the potential for development of nephritic syndrome. Additional sideeffects of Tiopronin include pancytopenia, nausea, vomiting,

gastrointestinal upset, rash, decreased taste sensation, and lupus-like symptoms, which limit its use in a substantial number of patients.

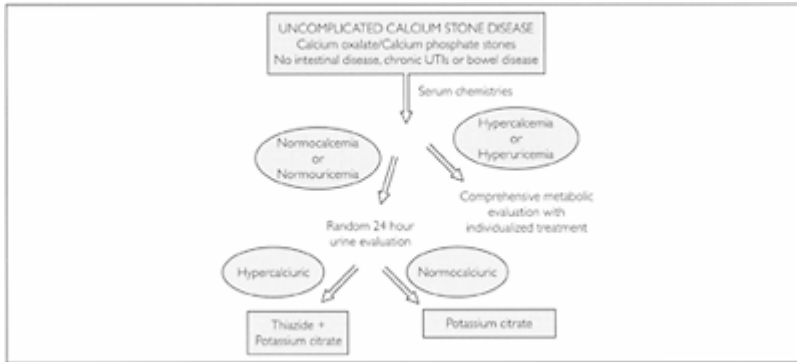
**Infection stones.** Struvite (magnesium ammonium phosphate) stones are associated with urinary infection with urea-splitting bacteria.<sup>47</sup> Because these stones harbor bacteria within the stone itself, the primary goal of therapy is eradication of the stone and elimination of the source of infection. Surgical stone removal and longterm antimicrobial prophylaxis constitute the mainstay of treatment.

Acetohydroxamic acid, a bacterial urease inhibitor, has been found to inhibit the growth of infection stones but its clinical use has been limited by a high incidence of sideeffects.<sup>133</sup> Williams and colleagues found that 50% of their patients required a decrease in dosage or cessation of treatment because of adverse effects, including tremulousness, thrombophlebitis, hemolytic anemia, and alopecia.<sup>133</sup> The starting dose of acetohydroxamic acid is 250 mg, three times daily, with an increase in dosage up to 500 mg, three times daily, as needed and tolerated. Urinary acidification with ammonium chloride (1.5–3 g/day) has also been reported with mixed results,<sup>134</sup> although no randomized trials have been performed.

### **Simplified approach to medical management**

In order to simplify the approach to management of the calcium stone-forming patient, Pak and Resnick offered a series of guidelines by which patients could be evaluated and classified into simple treatment groups.<sup>55</sup> In addition to a careful medical, dietary, and family history, the workup includes limited serum chemistries (creatinine, potassium, bicarbonate, calcium, phosphorus, uric acid, and intact PTH) and a single 24-hour urine collection obtained while the patient is on a random diet. Optionally, a second urine collection may be obtained after dietary modifications based on the findings of the first urine collection, such as increasing fluid for low urine volume, reducing salt intake for high urinary sodium, limiting animal protein for high uric acid, and lowering intake of oxalate-rich foods for a high urinary oxalate. This maneuver eliminates environmental influences on the urine stone risk profile.

Treatment recommendations based on this approach are limited to patients with ‘uncomplicated’ calcium stone disease, defined as formation of calcium oxalate or calcium phosphate stones in patients with associated normocalcemia and normouricemia who are without intestinal disease or a history of chronic urinary tract infections (Figure 26.1). Making the recommendations, Pak eliminated from consideration patients with primary



**Figure 26.1** Algorithm for treatment and evaluation of uncomplicated calcium stone disease. UTIs=urinary tract infections.

hyperparathyroidism, enteric hyperoxaluria, infection, uric acid, or cystine stones and patients with primary gout who are more appropriately managed with specific therapy aimed at the underlying disorder.

Patients are then stratified by urinary calcium status: hypercalciuric vs normocalciuric. The hypercalciuric group comprises patients with absorptive, renal, and dietary hypercalciuria. First-line therapy for this group is a thiazide diuretic (or indapamide) supplemented with potassium citrate. The normocalciuric group includes patients with hyperuricosuric, hypocitraturic, hypomagnesuric, and mild hyperoxaluric calcium oxalate nephrolithiasis; the preferred treatment for this group is potassium citrate. For patients who relapse despite these recommended treatments, the addition of specific therapy, such as allopurinol for patients with hyperuricosuria, may address the uncorrected urinary risk factor. This approach should provide a systematic evaluation and rational treatment plan that is achievable for all stone-forming patients by all health-care providers managing patients with kidney stones.

### Summary

In conclusion, the key to stone management is stone prevention. By understanding the underlying pathophysiologic abnormalities that predispose to stone formation and applying a rational diagnostic approach, the metabolic and environmental disorders can be addressed and corrected with a combination of dietary and drug therapy.

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## Shock wave lithotripsy for urinary stones and non-calculus applications

Kenneth Ogan and Margaret S Pea He

### Historical perspectives

Dornier, a German aerospace firm, first applied the principles of acoustical physics to the in-vitro fragmentation of kidney stones.<sup>1</sup> The electrohydraulic generator they developed created reproducible shock waves that fragmented kidney stones while sparing adjacent renal tissue. After success in a canine model, the first human lithotripter prototype, the HM1 (human machine), was introduced in 1980.

Chaussy and coworkers reported their early clinical experience with shock wave-induced kidney stone destruction in 1982.<sup>2</sup> Among 72 patients with renal calculi treated with 500–1000 shocks, 69 patients underwent post-treatment radiographic imaging and only 8.5% were found to have residual stone fragments. However, 2 patients with staghorn calculi and 2 patients with ureteral calculi failed shock wave treatment and subsequently required open surgical intervention. Although no major complications were reported, 15% of patients experienced renal colic with fragment passage. Of note, all patients underwent radionuclide imaging post-SWL (shock wave lithotripsy) and none showed a change in renal clearance.

The first commercial lithotripter, the Dornier HM3, became available in the United States in 1984. Since that time, several generations of lithotriptors have been introduced that differ in their means of shock wave generation and coupling as well as in the functionality of the table, all in an effort to increase successful stone fragmentation, decrease patient morbidity, and increase ease of use.

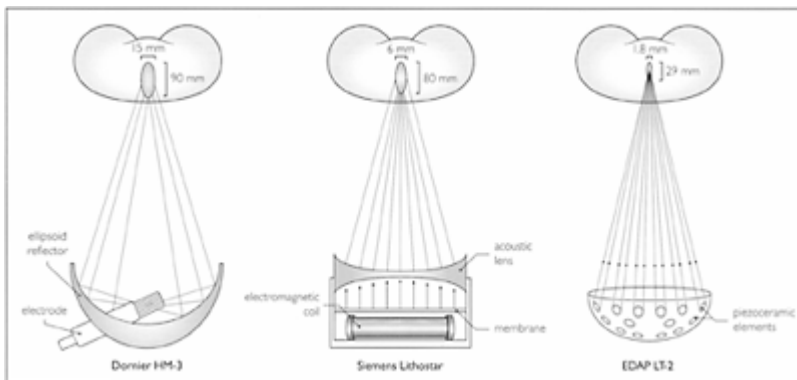
### Shock wave lithotripsy principles and lithotriptors

A lithotripter comprises a shock wave source, a mechanism for focusing the shock waves at a focal point, a coupling medium to allow propagation of the shock waves from the source to the patient without attenuation, and an imaging modality for stone localization and targeting.

#### *Shock wave generation*

The three commercially available shock wave sources are electrohydraulic (spark gap), electromagnetic, and piezoelectric (Figure 27.1). The first shock wave generator developed and subsequently used in the Dornier HM3 lithotripter was electrohydraulic.<sup>2</sup> This generator is considered a 'point source' generator because the shock waves diverge from a single source (the F1 focal point) and are reflected off an ellipsoid reflector before converging at a distant target (the F2 focal point). The shock wave is generated by the electrical discharge of an underwater spark-gap electrode, causing vaporization of water at the F1 focal point. The rapid gaseous expansion around the electrode then produces a shock wave that diverges from the point of origin and is reflected and focused at F2 (a second focal point) where the stone is positioned.<sup>3</sup> The distance between F2 and F1 is determined by the shape of the ellipsoid reflector, and, in the case of the Dornier HM3 lithotripter, is 15 cm. Although this generator has proven to be very effective in fragmenting stones, pressure fluctuations between shocks and a relatively short electrode life are minor disadvantages.<sup>4</sup>

Piezoelectric lithotripsy, developed in 1986,<sup>5</sup> relies on an 'extended source' generator, which creates a shock wave that is directly focused on the treatment point.<sup>3</sup> This system comprises an array of polarized polycrystalline ceramic elements lining a hemispheric dish, which simultaneously expand when a high voltage charge is applied, thereby producing a shock wave. The F2 focal point of piezoelectric generators is small, and consequently the low-energy level of the shock waves at the skin entry point is associated with little patient discomfort and minimal analgesic requirements. However, the small F2 volume also



**Figure 27.1** Schematic view of electrohydraulic, electromagnetic, and piezoelectric shock wave generators. The electrohydraulic generator uses an electrode to generate a shock wave that is focused by means of an ellipsoid reflector. The electromagnetic generator uses an electromagnetic coil

to generate a shock wave that is focused by means of an acoustic lens. The piezoelectric generator uses polycrystalline ceramic elements to generate a shock wave that is focused by means of the array of ceramic elements on a spherical dish.

necessitates continuous, precise targeting of the stone to maximize contact with the shock waves.

The electromagnetic generator, first reported in clinical use by Wilbert and associates in 1987, comprises a shock tube containing a metallic membrane surrounding a magnetic coil.<sup>6</sup> When an electrical charge is applied to the coil, the oppositely charged metallic membrane is repelled, thereby generating a shock wave that is focused at the F2 focal point by means of an acoustic lens. Like the piezoelectric generator, the electromagnetic generator has a small focal zone and a large skin entry site and is therefore associated with less pain than the electromagnetic lithotriptors. These generators require no disposable electrodes and are durable, requiring less frequent replacement of parts than the electrohydraulic generators.

A fourth type of lithotripter, based on a microexplosive generator, was developed by Kuwahara and coworkers in 1987, but is not currently commercially available.<sup>7</sup> This generator produces shock waves by the way of explosion of tiny lead azide pellets within a parabolic reflector. Experimentally, this generator has been effective at fragmenting stones, but concerns over handling of the volatile lead azide pellets have prevented its commercialization.

### *Shock wave focusing*

Point source generators utilize an ellipsoid reflector to direct the shock waves to the target (electrohydraulic), whereas extended source generators use an acoustic lens (electromagnetic and some piezoelectric) or a spherical dish for focusing (piezoelectric). Shock wave focusing devices are characterized by their aperture and focal zone. The shock wave aperture corresponds to the area of the acoustic lens, spherical dish, or ellipsoid reflector. Lithotriptors with wide apertures tend to have lower energy densities at skin level because the energy is distributed over a larger surface area.

The focal zone represents the actual volume into which the shock waves are concentrated. In general, larger focal zones are associated with greater shock wave energy and higher peak pressures and correlate with greater stone fragmentation, but also an increased risk of tissue damage.

### *Shock wave coupling*

Shock wave coupling refers to the medium through which shock waves travel to reach the target. The coupling medium is aimed at minimizing the shock wave attenuation that accompanies travel through an interface between differing acoustic densities. The initial

coupling medium on the Dornier HM3 lithotripter was degassed water, which has an acoustic impedance matched to soft tissues, housed within a large tub. Subsequently, the water bath was replaced with a water-filled cushion and applied ultrasound gel, or a shock tube that contained the shock wave source, water, and coupling membrane, which resulted in slightly more diminution of shock wave energy than the water bath. These 'dry' lithotriptors are more convenient and allow greater flexibility for patient positioning.<sup>4</sup>

### *Imaging*

The imaging modalities utilized for stone localization include real-time fluoroscopy, hard copy radiography, ultrasonography, and a combination of fluoroscopy and ultrasound. The original Dornier HM3 lithotripter utilized biplaner fluoroscopy, i.e. two X-ray units placed at right angles to each other, to localize stones at the F2 focal point. Lithotriptors like the Medstone STS utilize hard copy radiography to target the stone, with the disadvantage of needing to stop treatment to assess localization and progress. The biplaner system was subsequently replaced in newer-generation lithotriptors with a mounted C-arm fluoroscopic unit that could provide multiplaner imaging within a single system. Fluoroscopy provides reliable imaging of radiopaque calculi and can be used in conjunction with intravenous or instilled (antegrade or retrograde) iodinated contrast for hard-to-localize and radiolucent calculi. More recently, ultrasound imaging has been incorporated into many machines and offers the advantages of limiting ionizing radiation exposure, particularly in pediatric patients, and facilitating treatment of radiolucent calculi. However, ultrasound-based systems are unable to localize ureteral calculi except in cases where distal ureteral stones are outlined by the acoustic window of a full bladder.

Since the introduction of the first commercially available lithotripter, the Dornier HM3 in 1984, numerous fixed site and portable lithotriptors have been introduced and modified. Current lithotriptors and their characteristic features are listed in Table 27.1.

## **Preoperative evaluation and patient preparation**

### *History*

When obtaining a patient history, it is important to elicit information that may impact treatment selection or patient preparation. History of a bleeding disorder should prompt further hematologic evaluation, and if unable to be corrected, mandates an alternative treatment modality. Pregnancy is a contraindication to SWL treatment, and women of childbearing age should seek alternative treatment for stones in the mid or distal ureter because of the theoretical risk of injury to the ovary. A history of recurrent urinary tract infections may suggest the presence of infection stones and requires appropriate urine cultures and antibiotic pretreatment.

Knowledge of previous stone composition and the success of prior SWL treatments should be elicited as it may influence current treatment selection. A history of a cystinuria should preclude SWL treatment of stones >1 cm in size. Likewise, previous SWL failures might dissuade one from using SWL as first-line therapy.

### *Radiographic imaging*

Appropriate preoperative radiographic imaging is essential for safe, efficacious SWL treatment. Although computed tomography (CT) imaging is commonly used for the diagnosis of renal and ureteral calculi and provides a good estimation of stone burden and location, contrast imaging such as the intravenous urogram is recommended to assess grossly the functional status of the kidney and the anatomy of the collecting system and ureter.

### *Laboratory studies*

Preoperative laboratory evaluation should, at minimum, include hemoglobin, creatinine, and potassium to establish baseline renal function and blood count. Other serum chemistries, such as bicarbonate, calcium, uric acid, phosphorus, and intact parathyroid hormone, are suggested to rule out a systemic cause of stone disease, but are not essential for SWL treatment.

Documentation of sterile urine is mandatory. Patients with infected urine should be treated for 7–10 days with culture-specific antibiotics prior to SWL; likewise, patients with suspected infection-related stones should be pretreated with culture-specific or broad-spectrum anti-biotics for 2 weeks prior to SWL treatment and should receive appropriate intravenous antibiotics at the time of the procedure. The need for routine preprocedure anti-biotics in patients with a sterile preoperative urine culture has been questioned, and there is no uniform consensus in the literature regarding the ideal antibiotic regimen.<sup>8</sup>

### *Patient preparation*

For patients with small or faintly opaque calculi, it is beneficial to administer a mechanical bowel preparation the day prior to the procedure to minimize the effect of overlying bowel on stone visualization and targeting.

### **Anesthesia**

Although SWL treatment with the first-generation Dornier HM3 lithotripter initially involved the use of

**Table 27.1** *Lithotripter characteristics (modified from Lingeman et al.<sup>182)</sup>*

| Company                 | Machine   | Focusing  | Aperture (cm) | Focal zone (W X L mm) | Peak pressure at focal point (bar) | Electrode life span (SW) | Imaging |
|-------------------------|-----------|-----------|---------------|-----------------------|------------------------------------|--------------------------|---------|
| <i>Electrohydraulic</i> |           |           |               |                       |                                    |                          |         |
| Medispec                | Econolith | Ellipsoid | 17.6          | 13×60                 | N/A                                | 3000                     | X-ray,  |

| Ltd.                    | reflector                     |                                      |                |               |                       |                   | portable C-arm, optional US                     |
|-------------------------|-------------------------------|--------------------------------------|----------------|---------------|-----------------------|-------------------|---|
| Medispec Ltd.           | Econolith 2000                | Ellipsoid reflector                  | 17.1, 17.6, 22 | 13×60 or 6×26 | N/A                   | 3000              | X-ray, portable C-arm, optional US              |
| Healthtronics           | Litho Iron                    | Ellipsoid reflector                  | 20             | 8×38          | 530 <sup>a</sup>      | 8000              | X-ray, portable C-arm                           |
| Healthtronics           | Litho Iron Ultra              | Ellipsoid reflector                  | 20             | 8×38          | 530 <sup>a</sup>      | 8000              | X-ray   |
| Comair AB               | Lithocut C-3000S <sup>b</sup> | Ellipsoid reflector                  | 23             | 3.5×12        | 1200                  | Approx 5 sessions | X-ray, optional US                              |
| Medirex Systems Corp.   | Tripter X-1 Compact           | Ellipsoid reflector                  | 18.1           | 13×48         | 400–1100 <sup>C</sup> | 3000              | X-ray, portable C-arm, fluoroscopy              |
| Direx Medical Systems   | Compact <sup>b</sup>          | Interchangeable ellipsoid reflectors | 18.1, 13, 24   | 13×48         | 400–1100 <sup>C</sup> | 3–12,000          | X-ray, portable C-arm, fluoroscopy, optional US |
| Direx Medical Systems   | Nova <sup>b</sup>             | Interchangeable ellipsoid reflectors | 18.1, 13, 24   | 13×48         | 400–1100 <sup>C</sup> | 3–12,000          | X-ray, portable C-arm, fluoroscopy, optional US |
| Direx Medical Systems   | Nova Ultima <sup>b</sup>      | Ellipsoid reflector                  | 18.1           | 13×48         | 400–1100 <sup>C</sup> | 3–12,000          | X-ray, portable C-arm, fluoroscopy, optional US |
| EDAP Technomed          | Sonolith Praktis <sup>b</sup> | Ellipsoid reflector                  | 28             | 12×23         | N/A                   | 12,000            | X-ray, US                                       |
| EDAP Technomed          | Sonolith 3000a–d              | Ellipsoid reflector                  | 26             | 15×55         | N/A                   | 200,000           | US  |
| EDAP Technomed          | Sonolith 4000 <sup>a-d</sup>  | Ellipsoid reflector                  | 28             | 12×23         | N/A                   | 12,000            | X-ray, US                                       |
| Medstone International  | STS                           | Ellipsoid reflector                  | 15             | 13×50         | N/A                   | 3600              | X-ray, US                                       |
| Medstone International  | STS-T                         | Ellipsoid reflector                  | 15             | 13×50         | N/A                   | 3600              | X-ray   |
| Dornier Medical Systems | HM3 <sup>d</sup>              | Ellipsoid reflector                  | 15.6, 17.2     | 15×90         | 220–360               | 2000              | X-ray   |
| Dornier Medical Systems | MFL 5000 <sup>d</sup>         | Ellipsoid reflector                  | 17.2           | 10×40         | 290–390 <sup>a</sup>  | 2500              | X-ray, optional US                              |

|                           |                              |   |              |        |                         |                     |   |
|---------------------------|------------------------------|---|--------------|--------|-------------------------|---------------------|---|
| PCK Co., Ltd.             | Stonolith <sup>b</sup>       | Interchangeable ellipsoid reflectors    | 17, 17.6, 22 | 7.7×30 | N/A                     | 150,000             | X-ray, optional US                      |
| PCK Co., Ltd.             | Stonolith Smart <sup>b</sup> | Interchangeable ellipsoid reflectors    | 17, 17.6, 22 | 7.7×30 | N/A                     | 150,000             | X-ray, optional US                      |
| ELMED Lithotripsy Systems | Multimed 2001 <sup>b</sup>   | Ellipsoid reflector                     | 17.6         | 7.5×22 | N/A                     | 4500                | X-ray, US                               |
| ELMED Lithotripsy Systems | Complit <sup>b</sup>         | Isoscentric movable ellipsoid reflector | 17.6         | 7.5×22 | N/A                     | 4500                | X-ray, US                               |
| <i>Electromagnetic</i>    |                              |   |              |        |                         |                     |   |
| Siemens Medical Systems   | Lithostar Modularis          | Acoustic lens                           | 14.4         | 6×80   | 500 <sup>a</sup>        | 750,000             | X-ray                                   |
| Siemens Medical Systems   | Lithostar Modularis          | Acoustic lens                           | 17           | 5×80   | 800 <sup>a</sup>        | 2 million           | X-ray, coaxial US                       |
| Karl Storz Lithotripsy    | Modulith SL20*               | Parabolic reflector                     | 30           | 3×37   | 1056 <sup>a</sup>       | 6 million           | X-ray, coaxial US                       |
| Karl Storz Lithotripsy    | Modulith SLX                 | Parabolic reflector                     | 30           | 3×37   | 1056 <sup>a</sup>       | 8 million           | X-ray, coaxial US                       |
| Karl Storz Lithotripsy    | Modulith SLX-T               | Parabolic reflector                     | 30           | 3×37   | 1056 <sup>a</sup>       | 8 million           | Mobile C-arm X-ray, coaxial US          |
| Dornier Medical Systems   | Compact-S <sup>d</sup>       | Acoustic lens                           | 14           | 6.4×70 | 460 <sup>a</sup>        | 600,000             | X-ray, optional US                      |
| Dornier Medical Systems   | DoLi/50 <sup>d</sup>         | Acoustic lens                           | 14           | 6.4×70 | 460 <sup>a</sup>        | 600,000             | X-ray                                   |
| Dornier Medical Systems   | DoLi S                       | Acoustic lens                           | 22           | 5×45   | 166–7 <sup>a</sup> 15 • | 600,000             | X-ray, optional US                      |
| Dornier Medical Systems   | Compact Delta                | Acoustic lens                           | 14           | 7.7×81 | 210–556 <sup>a</sup>    | 600,000             | X-ray, optional US                      |
| <i>Piezoelectric</i>      |                              |   |              |        |                         |                     |   |
| EDAP Technomed            | LT.02 <sup>d</sup>           | Spherical dish                          | 29           | 1.8×29 | 1400                    | Individual crystals | Coaxial x-ray and US replaced as needed |

<sup>a</sup> PVDF measurements.

<sup>b</sup> Not FDA approved.

<sup>c</sup> Piezoelectric measurements.

<sup>d</sup> No longer manufactured. US, ultrasound.

general or regional anesthesia, investigators have subsequently shown that intravenous sedation using a combination of midazolam and alfentanil or fentanyl and propofol provides adequate patient anesthesia even when using the unmodified Dornier HM3 lithotripter.<sup>9</sup> Nevertheless, the impetus for the development of second- and third-generation lithotriptors was the potential for reduced anesthesia requirements using smaller focal zones and larger ellipsoid reflectors.



Narcotic analgesics administered during SWL treatment have been shown to produce better pain relief and result in greater patient satisfaction when delivered via a patient-controlled analgesia (PGA) device.<sup>10</sup> However, local anesthetic alone<sup>11</sup> or in combination with nonsteroidal anti-inflammatory drugs (NSAIDs)<sup>12</sup> may obviate the need for parenteral narcotics altogether. In a study using the MPL9000, NSAIDs alone were sufficient to produce adequate pain relief in 80% of patients. Topical agents such as EMLA cream (a combination of lidocaine and prilocaine) have also been shown to decrease anesthetic requirements during SWL.<sup>13</sup> Finally, it has been suggested that for distal ureteral stones, SWL treatment may not require any anesthesia. Jermini and associates, treating 165 patients with distal ureteral calculi on a Lithostar Ultra lithotripter, found that 93% of patients were able to tolerate the procedure without any need for anesthesia or analgesia.<sup>14</sup>

Despite the efforts of investigators to reduce anesthesia requirements and cost with newer-generation lithotriptors, there is recent evidence that these measures may also reduce the effectiveness of SWL treatment. In a retrospective review of 295 patients treated with the Doli 50 lithotripter, 55% of 60 patients treated with intravenous sedation vs 87% of 126 patients treated with general anesthesia were rendered stone free at 3 month follow-up, leading these authors to paradoxically recommend the use of general anesthesia for SWL treatment with this third-generation lithotripter.<sup>15</sup>

### Outcomes for renal stones

In the first clinical report of SWL treatment of renal pelvic calculi by Chaussy and associates in 1980 a success rate of 95% (20 of 21) was reported. Since that time over 500,000 SWL treatments on the Dornier HM3 lithotripter have been reported worldwide.<sup>17</sup> Success rates, retreatment rates, and auxiliary procedures rates have ranged from 44 to 90%, 4 to 20%, and 3 to 30%, respectively, in several large series (Table 27.2). The outcomes for second- and third-generation lithotriptors for the treatment of renal calculi are often inferior to those reported for the Dornier HM3 lithotripter and are listed in Table 27.3.

**Table 27.2** *Treatment results with Dornier HM3: nonstaghorn renal calculi*

| Authors                                    | n                 | Stone free      | Retreatment    | Auxiliary procedures |
|--|-------------------|-----------------|----------------|----------------------|
| Chaussy and Schmiedt <sup>105</sup> (1983) | 498 <sup>a</sup>  | 90% (419/446)   | 12% average    | —                    |
| Drach et al <sup>17</sup> (1986)           | 2112 <sup>b</sup> | 66% (610/919)   | 16% (338/2112) | 8% (205/2501)        |
| Lingeman et al <sup>183</sup> (1986)       | 982 <sup>c</sup>  | 72% (407/569)   | 10% (103/982)  | 16% (153/982)        |
| Palfrey et al <sup>184</sup> (1986)        | 654 <sup>d</sup>  | 44% (141/320)   | 14% (45/320)   | 20% (64/320)         |
| Riehle et al <sup>185</sup> (1986)         | 467 <sup>e</sup>  | 75% (224/300)   | 5% (26/518)    | 30% (156/518)        |
| Das et al <sup>186</sup> (1987)            | 1000 <sup>d</sup> | 85% (642/751)   | 4% (39/1000)   | 8% (82/1000)         |
| Politis and Griffith <sup>195</sup> (1987) | 1060              | 74% (641/863)   | 8% (92/1128)   | 6% (63/1128)         |
| Mays et al <sup>19</sup> (1988)            | 933 <sup>f</sup>  | 45% (334/746)   | 8% (72/933)    | 4% (37/933)          |
| Rigatti et al <sup>23</sup> (1989)         | 2557 <sup>g</sup> | 72% (1044/1443) | 20% (514/2526) | 26% (663/2557)       |
| Cass et al <sup>20</sup> (1995)            | 3121              | 70% (1670/2402) | 4% (136/3121)  | 3% (74/2402)         |

Overall 13,384 70% (6132/8779) 14% (1365/9640) 12% (1506/12,341)

<sup>a</sup> Includes 32 patients with ureteral stones.

<sup>b</sup> Includes 14% with staghorn and ureteral calculi.

<sup>c</sup> Includes 194 ureteral stones.

<sup>d</sup> Includes patients with ureteral stones.

<sup>e</sup> Includes some patients with ureteral and staghorn stones.

<sup>f</sup> Includes 112 patients with staghorn calculi and at least 20 patients with ureteral stones.

<sup>g</sup> Includes staghorn and ureteral stones, but stone-free rate includes only renal stones.

**Table 27.3** *Treatment result for second- and third-generation lithotriptors for treatment of nonstaghorn renal calculi*

| Author                                    | Lithotripter           | n                    | Stone free       | Retreatment               | Auxiliary procedures |
|---|------------------------|----------------------|------------------|---------------------------|----------------------|
| <i>Electrohydraulic</i>                   |                        |                      |                  |                           |                      |
| Graff et al <sup>187</sup> (1989)         | Dornier MFL 5000       | 265                  | 68%              | 14% 2% post               |                      |
| Talati et al <sup>188</sup> (1991)        | Dornier MFL 9000       | 464 <sup>a</sup>     | 73%              | 46% 9% post               |                      |
| Cass <sup>189</sup> (1991)                | Medstone STS           | 480 <sup>b</sup>     | 64%              | 6% 2.5% post              |                      |
| Swanson et al <sup>190</sup> (1992)       | Northgate SD-3         | 281                  | 58%              | 9% 5%                     |                      |
| Simon <sup>191</sup> (1995)               | Medispec Econolith     | 500                  | 75%              | 8%                        |                      |
| Elhilali et al <sup>192</sup> (1996)      | Dormer Compact Delta   | 169                  | 73%              | 13% 2.4%                  |                      |
| Lalak et al <sup>22</sup> (2002)          | Dornier Compact Delta  | 467                  | 68%              | 24% pre, 6% post          |                      |
| <i>Electromagnetic</i>                    |                        |                      |                  |                           |                      |
| Wilbert et al <sup>193</sup> (1987)       | Siemens Lithostar      | 698 <sup>c</sup>     | 65%              | 12% 12%                   |                      |
| Clayman et al <sup>16</sup> (1989)        | Siemens Lithostar      | 266 <sup>d</sup>     | 71%              | 7% 16%                    |                      |
| el-Damanhoury et al <sup>194</sup> (1991) | Siemens Lithostar      | 2117                 | 65%              | 11% pre, 2% post          |                      |
| el-Damanhoury et al <sup>194</sup> (1991) | Siemens Lithostar Plus | 25                   | 100%             | 20% 16%                   |                      |
| Kohrman et al <sup>195</sup> (1991)       | Stortz Modulith SL20   | 185 <sup>h</sup>     | 83%              | 19% 16%                   |                      |
| Psihramis et al <sup>196</sup> (1992)     | Siemens Lithostar      | 1000 <sup>e</sup>    | 52%              | 19% –                     |                      |
| Listen et al <sup>197</sup> (1992)        | Stortz Modulith SL20   | 500 <sup>g</sup>     | 78%              | 32% 20% pre, 4.6% post    |                      |
| Mobley et al <sup>198</sup> (1993)        | Siemens Lithostar      | 1 1,516 <sup>f</sup> | 69%              | 16% 28.5% pre, 3.7% post  |                      |
| Coz et al <sup>21</sup> (2000)            | Stortz Modulith SL20   | 828 calculi          | 87%              | 21% –                     |                      |
| <i>Piezoelectric</i>                      |                        |                      |                  |                           |                      |
| Vallancien et al <sup>199</sup> (1988)    | EDAP LT01              | 386                  | 74% <sup>k</sup> | 14% –                     |                      |
| Bowsher et al <sup>200</sup> (1989)       | Wolf Piezolith         | 398                  | 53%              | 62% 15% post              |                      |
| Rassweiler et al <sup>201</sup> (1989)    | Wolf Piezolith 2200    | 378 <sup>i</sup>     | 72%              | 45% 14.8% pre, 14.3% post |                      |
| Miller et al <sup>202</sup> (1989)        | EDAP LT01              | 461                  | 51%              | –                         |                      |

| Tan et al <sup>203</sup> (1990)     | EDAP LT01               | 180j | 64%        | 40% 15% post |                      |
|-------------------------------------|-------------------------|------|------------|--------------|----------------------|
| Cope et al <sup>204</sup> (1991)    | Wolf Piezolith          | 220  | 75%        | 51% 4%       |                      |
| Author                              | Lithotripter            | n    | Stone free | Retreatment  | Auxiliary procedures |
| Lauganieta <sup>205</sup> (1991)    | Diasonics<br>Therasonic | >600 | 61%        | 23% –        |                      |
| Mykulak et al <sup>206</sup> (1992) | Diasonics<br>Therasonic | 130  | 57%        | 21% –        |                      |

<sup>a</sup> Includes 48 ureteral stones; stone free for renal only.

<sup>b</sup> Includes 43 staghorn and ureteral stones.

<sup>c</sup> Includes 182 ureteral stones.

<sup>d</sup> Includes 16% ureteral stones.

<sup>e</sup> Includes 164 ureteral stones; stone free for renal only.

<sup>f</sup> Includes 365 branched stones.

<sup>g</sup> Includes 120 ureteral stones.

<sup>h</sup> Includes 34% ureteral stones.

<sup>i</sup> Includes 103 staghorn and ureteral stones.

<sup>j</sup> Includes 43 staghorn and ureteral stones.

<sup>k</sup> Stone free plus clinically insignificant fragments.

Stone-free rate is only one of several factors that contribute to overall treatment efficacy. Retreatment rates and need for auxiliary procedures are important variables that affect the overall efficiency of a given machine. Clayman and associates developed the concept of an 'efficiency quotient' (EQ) to take into account all the variables that determine overall lithotripter efficacy:<sup>16</sup>

$$EQ = \frac{\% \text{ stone free}}{(100\% \text{ initial SWL session} + \% \text{ SWL retreatment} + \% \text{ secondary procedures})}$$

According to this formula, the ideal lithotripter would have an EQ equal to 1, corresponding to a 100% stone-free rate in a single treatment session without the need for any ancillary procedures.

The success of SWL depends on a number of factors, including stone size, stone location, stone composition, and type of lithotripter. Most studies have shown that stone-free rates vary inversely with stone size (Table 27.4). For stones <2 cm in size, stone-free rates range from 59% to 92%. However, for stones >2 cm, stone-free rates vary from 39% to 81%.<sup>17–23</sup> Moreover, Lingeman and associates found that the retreatment rate and need for ancillary procedures increased from 7% to 33% and from 11% to 27%, respectively, when comparing treatment of stones <2 cm with those >2 cm.<sup>24</sup> Politis and Griffith also noted a 3-fold higher complication rate when treating stones >1.5 cm compared with those <1.5 cm.<sup>25</sup>

Stone location also influences treatment outcomes, primarily as a result of differential clearance of stone fragments from different renal locations (Table 27.5). Renal pelvic stones are associated with a higher success rate with SWL treatment than calyceal stones, with lower calyceal stones associated with the poorest stone-free rates. In 1060 patients with solitary renal calculi treated with SWL, Politis and Griffith reported a stone-free rate

of 81% vs 69% for renal pelvic and caliceal stones, respectively.<sup>25</sup> Lower calyceal stones had the lowest stone-free rate at 65%.

Because of the observed difference in stone-free rates for SWL treatment of stones in the lower pole calyces compared with stones elsewhere in the kidney, Lingeman and colleagues performed a meta-analysis of series in the literature for which outcomes for SWL and percutaneous nephrolithotomy (PCNL) were stratified by stone location.<sup>26</sup> Overall, they found that SWL was associated with a 60% stone-free rate compared with 90% for PCNL. As expected, SWL stone-free rates varied inversely with stone size: 74% for stones  $\leq 10$  mm, 56% for stones 11–20 mm, and 33% for stones  $>20$  mm. In contrast, PCNL stone-free rates showed very little size dependence and were uniformly high regardless of stone size.

Prompted by the results of the meta-analysis, a multicenter, prospective, randomized trial comparing SWL with PCNL for the treatment of lower pole calculi was initiated.<sup>27</sup> Among 107 patients with adequate 3-month followup, an overall stone-free rate of 37% for SWL and 95% for PCNL was achieved. The SWL stone-free rates for stones between 1 and 2 cm were only 23% and for stones between 2 and 3 cm only 14%.<sup>27</sup> In contrast, PCNL stone-free rates were 92–100%, with little difference based on stone size.

The poor clearance of fragments from the lower pole following SWL has been attributed to unfavorable anatomic features associated with the lower calyceal system. Sampaio and Aragao theorized that the lower pole infundibulopelvic angle and infundibular length as well as the spatial configuration of the lower pole calyces all play a role in facilitating or hindering clearance of fragments from the lower pole after SWL. They suggested that poor stone clearance was associated with a lower pole

**Table 27.4** *SWL stone-free rates for renal calculi stratified by size*

| Authors                            | Lithotripter          | Stone size      |                 |                |
|------------------------------------|-----------------------|-----------------|-----------------|----------------|
|                                    |                       | $<1$ cm         | 1–2 cm          | $>2$ cm        |
| Drach et al <sup>17</sup> (1986)   | Dornier HM3           | 83% (213/258)   | 79% (231/293)   | 53% (21/40)    |
| Kulb et al <sup>18</sup> (1986)    | Dornier HM3           | 77% (170/221)   | 75% (209/280)   | 43% (26/61)    |
| Mays et al <sup>19</sup> (1988)    | Dornier HM3           | 64% (6/25)      | 59% (210/356)   | 39% (17/44)    |
| Rigatti et al <sup>23</sup> (1989) | Dornier HM3           | 92% (447/286)   | 89% (514/577)   | 70% (258/368)  |
| Cass <sup>20</sup> (1995)          | Dornier HM3           | 75% (1124/1502) | 62% (444/716)   | 55% (102/184)  |
| Cass <sup>20</sup> (1995)          | Medstone STS          | 79% (1461/1856) | 63% (551/874)   | 50% (102/204)  |
| Coz et al <sup>21</sup> (2000)     | Modulith SL-20        | 87% (201/230)   | 88% (276/315)   | 81% (57/70)    |
| Lalak et al <sup>22</sup> (2002)   | Dornier Compact Delta | 76% (160/210)   | 66% (153/232)   | 47% (27/58)    |
| Total                              |                       | 84% (3872/4588) | 71% (2588/3643) | 59% (610/1029) |

**Table 27.5** *SWL stone-free rates for renal calculi stratified by location*

| Authors                          | Lithotripter | Stone location |             |              |              |
|----------------------------------|--------------|----------------|-------------|--------------|--------------|
|                                  |              | Renal pelvis   | Upper calyx | Middle calyx | Lower calyx  |
| Drach et al <sup>17</sup> (1986) | Dornier HM3  | 84% (263/313)  | 64% (25/39) | 73% (24/33)  | 73% (96/132) |
| Riehle et al <sup>185</sup>      | Dornier HM3  | 91% (83/91)    | 50% (2/4)   | 56% (5/9)    | 91% (21/23)  |

|   |                       |                 |               |                |                 |
|---|-----------------------|-----------------|---------------|----------------|-----------------|
| (1986)                                    |                       |                 |               |                |                 |
| Politis and Griffith <sup>25</sup> (1987) | Dornier HM3           | 81% (317/394)   | 82% (52/63)   | 72% (67/93)    | 65% (205/313)   |
| Mays et al <sup>19</sup> (1988)           | Dornier HM3           | 54% (60/111)    | 47% (25/53)   | 53% (35/58)    | 52% (67/130)    |
| Graff et al <sup>35</sup> (1988)          | Dornier HM3           | 84% (131/157)   | 78% (77/98)   | 76% (78/103)   | 58% (81/141)    |
| Rigatti et al <sup>23</sup> (1989)        | Dornier HM3           | 81% (464/573)   | 75% (171/228) | 66% (173/262)  | 62% (236/380)   |
| Cass <sup>20</sup> (1995)                 | Dornier HM3           | 70% (885/1258)  | 69% (119/172) | 75% (163/218)  | 67% (503/754)   |
| Cass <sup>20</sup> (1995)                 | Medstone STS          | 72% (1116/1541) | 68% (118/173) | 76% (191/252)  | 71% (689/968)   |
| Coz et al <sup>21</sup> (2000)            | Modulith SL-20        | 86% (209/243)   | 89% (58/65)   | 91% (105/116)  | 85% (162/191)   |
| Lalak et al <sup>22</sup> (2002)          | Dornier Compact Delta | 73% (80/109)    | 67% (42/63)   | 73% (47/64)    | 66% (150/227)   |
| Total                                     |                       | 75% (3608/4790) | 72% (689/958) | 74% (888/1208) | 68% (2210/3259) |

infundibulopelvic angle  $<90^\circ$ , an infundibular width  $<4$  mm and multiple, separate, lower pole calyces.<sup>28</sup> In a prospective trial of 74 patients with lower pole stones treated with SWL, Sampaio and colleagues reported a stone-free rate of 72% (39 of 52) in patients with an infundibulopelvic angle  $>90^\circ$  compared with 23% (5 of 22) in patients with an angle  $<90^\circ$ .<sup>29</sup>

Other retrospective analyses have supported the findings of Sampaio and coworkers. Elbahnasy and colleagues found lower pole infundibulopelvic angle, infundibular width, and infundibular length to be significant predictors of stone clearance. In a retrospective study of 120 patients undergoing SWL treatment of lower pole stones  $<1.5$  cm in diameter, those with all three favorable anatomic parameters (infundibulopelvic angle  $>90^\circ$ , infundibular length  $<3$  cm, infundibular width  $>5$  mm) attained a 100% stone-free rate compared with a 16% stone-free rate when all anatomic factors were unfavorable (infundibulopelvic angle  $<40^\circ$ , infundibular length  $>3$  cm, infundibular width  $<5$  mm).<sup>30</sup> For patients with an infundibulopelvic angle  $>70^\circ$ , stone-free rates between 67% and 91% could be achieved depending on the combination of other anatomic factors. Likewise, Gupta and coworkers correlated stone-free rates with infundibulopelvic angle in 88 patients undergoing SWL for lower pole stones.<sup>31</sup> In 73% of successful cases, the lower pole angle was  $>45^\circ$ , and improved stone clearance occurred when the infundibular length was less than 3 cm.

Several other groups of investigators also identified infundibulopelvic angle as a predictor of success for SWL treatment of lower pole stones. Keeley and associates found infundibulopelvic angle to be the only significant anatomic factor to effect stone clearance after SWL; a stone-free rate of 66% was achieved in patients with an infundibulopelvic angle  $>100^\circ$  compared with only 34% in patients with an angle  $<100^\circ$ .<sup>32</sup> However, patients with all 3 negative anatomic factors (infundibulopelvic angle, infundibular length, and infundibular width) had a significantly lower stone-free rate of 9% compared with 71% if all factors were positive. Likewise, Sakkas and Boulinakis<sup>33</sup> and Pacik and Hanak<sup>34</sup> found that the infundibulopelvic angle was significantly greater in patients rendered stonefree compared with those left with residual fragments after SWL.

In both studies, although the lower pole infundibulum was shorter and wider in the stone-free group compared to the group with residual fragments, the differences were not statistically significant.

Not all investigators agree that lower pole calyceal anatomy influences outcomes after SWL. Albala and colleagues found no significant difference in the mean infundibulopelvic angle, infundibular length, and infundibular width between 21 SWL failures and 17 successes.<sup>27</sup> Despite the differences in findings among these studies, it is likely that lower pole calyceal anatomy plays some role in stone clearance after SWL, although the exact cut-points and role of each of the anatomic factors have yet to be determined.

Stone composition is also an important determinant of SWL success, with some stones more resistant to the effects of shock wave treatment than others. Calcium oxalate dihydrate, one of the most common stone types, fragments well with SWL. In a study by Graff and associates of 947 patients treated with SWL for which stones were available for analysis, stone-free rates for calcium oxalate and uric acid were 81% and 83%, respectively. However, cystine and struvite stones were associated with stone-free rates of only 60% and 63%, respectively.<sup>35</sup> Dretler and colleagues evaluated retreatment rates in patients with stones 1–3 cm in size treated with SWL and found the highest retreatment rates for calcium oxalate monohydrate (10.3%), followed by struvite (6.4%), and calcium oxalate dihydrate (2.8%).

Cystine stones are relatively resistant to the effects of shock waves. Hockley and associates reviewed their series of 43 patients with cystine stones treated with either SWL or PCNL.<sup>36</sup> For SWL-treated patients with stones <2 cm, a 71% stone-free rate was achieved compared with a 40% stone-free rate for stones >2 cm. In contrast, PCNL stone-free rates of 100% and 92% for cystine stones <2 cm and >2 cm, respectively, were achieved. Consequently, for patients with known cystine or calcium oxalate monohydrate stones >1 cm in size, alternative treatment modalities should be considered unless SWL has been known to be successful in the past.

Although stone-free status is generally considered the standard for determining the success of SWL treatment, there is a lack of uniformity in the literature as to what constitutes a successful treatment. A number of investigators have used stone free plus 'clinically insignificant residual fragments' (CIRF) to represent successful SWL treatment, with varying stone size cut-offs for CIRF. However, Stroom and colleagues have shown that the term 'clinically insignificant residual fragments' is inappropriate since the fate of these fragments is frequently not insignificant.<sup>37</sup> Among 160 patients left with <4 mm residual fragments after SWL of renal calculi and followed for a mean of 23 months (range 2–89 months), only 24% ultimately became stone free. Conversely, 60% of patients demonstrated either no change (42%) or an increase (18%) in stone burden at last follow-up. In addition, 43% of patients either experienced an episode of renal colic or required intervention at a mean follow-up of 26 months.

In a similar study by Khaitan and coworkers, 81 patients with <4 mm residual fragments after SWL treatment were followed for a mean of 15 months.<sup>38</sup> Only 24% of patients ultimately became stone free and 59% developed complications, over half (52%) of whom required additional operative intervention. Clinically significant episodes tended to occur in patients with large stone fragments, multiple stones, or calyceal stones. Consequently, despite the variability in the literature, SWL outcomes should be

expressed as stone-free rates only, although, admittedly, stone-free rates will depend on the sensitivity of the imaging modality used for follow-up.<sup>39</sup>

Early in the history of SWL treatment of renal calculi, ureteral stents were commonly placed prior to treatment to prevent obstruction from fragments as they passed. The role of ureteral stents in preventing complications and facilitating passage of fragments has been explored in several prospective, randomized trials. Bierkens and colleagues found no benefit from ureteral stent placement prior to SWL with respect to stone-free rate when treating stones >20 mm in size.<sup>40</sup> Likewise, Pryor and Jenkins found no difference in stone-free rates for 50 patients with stones between 7 and 25 mm with or without the use of ureteral stents.<sup>41</sup> However, in 27% of stented patients, the stents had to be removed early due to patient symptoms. Libby and colleagues also reported comparable stone-free rates, complications rates, and auxiliary procedure rates for stones between 1.5 and 3 cm treated with SWL with or without a stent, but noted a higher complication rate and need for auxiliary procedures in patients with stones >2.5 cm treated without a stent in place.<sup>42</sup> In addition, Preminger and coworkers treated 302 patients with <3 cm renal calculi and found no difference in stone-free rates between the stented and unstented groups but did note that patients in the stented group experienced more bladder and flank symptoms than the unstented group.<sup>43</sup>

In contrast to the previous studies showing no advantage to stent placement in patients with stones <3 cm, Chandhoke and coworkers prospectively randomized 97 patients with solitary 10–20 mm renal calculi or <20 mm proximal ureteral calculi undergoing SWL on a Dornier HM3 to no stent, a 4.7F stent, or a 7F stent and found no difference in stone-free or retreatment rates between the three groups. However, they noted significantly fewer emergency room visits in the stented groups and rehospitalizations in the 4.7F stent group compared with the unstented group. As expected, symptom scores were higher in the stented groups than in the unstented group.<sup>44</sup> Considering all the above studies, however, there appears to be little advantage to stent placement prior to SWL for renal calculi <2.5 cm in size, although for large-volume stones, stent placement may reduce complications and the need for secondary procedures.

### Outcomes for ureteral stones

Initial indications for SWL treatment included renal and proximal ureteral calculi only. The Dornier HM3 lithotripter did not easily accommodate treatment of stones in the middle or distal ureter because of problems visualizing, targeting, and accessing stones in these locations. The anterior location of stones in the middle ureter often precluded positioning at the F2 focal point, and attenuation of shock waves by the pelvic bone potentially rendered treatment ineffective. Likewise, shock wave access to stones in the distal ureter was precluded by the pelvic bone and limited when patients were positioned on the standard gantry. To overcome these problems, prone positioning for stones in the middle ureter and supine positioning for stones in the distal ureter using a modified Stryker frame allowed shock wave entry directly from the anterior approach for middle ureteral stones and through the obturator foramen or greater sciatic notch for distal ureteral stones.<sup>45</sup> In this way, stones in virtually any location in the ureter could be accessed and treated with SWL.

Proximal ureteral stones were initially displaced into the kidney prior to SWL treatment because of the theory that an 'expansion chamber' was necessary to provide adequate space around the stone for fragmentation.<sup>46</sup> Consequently, proximal and in some cases middle ureteral stones were manipulated into the kidney or bypassed with a ureteral catheter prior to SWL treatment. Although it initially appeared that SWL treatment was more successful after stone manipulation than in-situ, later series using higher energy and greater number of shock waves demonstrated comparable stone-free rates for in-situ and push-back or bypass SWL treatment. Furthermore, series showing inferior stone-free rates for in-situ SWL compared with pushback or stent bypass SWL probably suffered from selection bias in that stones treated in situ were usually those that were impacted and could not be manipulated into the kidney or bypassed with a stent. Indeed, several prospective randomized trials showed no statistically significant differences in stone-free rates for in-situ vs manipulated stones.<sup>47,48</sup> Consequently, current guidelines recommend in-situ SWL for treatment of proximal ureteral stones, with preplacement of a ureteral stent reserved for cases of complete ureteral obstruction, persistent pain, obstructive pyelonephritis, or perhaps large stones (>1.5 cm). A review of the Dornier HM3 series of SWL for proximal ureteral stones reveals a mean stone-free rate of 79% (range 73–96%) with retreatment rates of 0–27%. For second- and third-generation lithotriptors, the mean stone-free rate is 84% (range 59–96%), with retreatment rates of 4–31% (Table 27.6).

Middle ureteral stones are difficult to visualize and target due to the superimposed pelvic bone. As such, most series of SWL treatment for middle ureteral stones reflect a high proportion of patients treated with stent bypass. Overall, stone-free rates of 83% (range 53–97%) for Dornier HM3 SWL and 79% (range 51–100%) for newergeneration lithotriptors have been achieved. Mean retreatment rates are 18% and 31%, respectively, for first- and higher-generation lithotriptors (see Table 27.6).

Distal ureteral stones represent an area of great controversy with regard to optimal management. Because of the high success rates and low complication rates with

**Table 27.6** *Treatment results for ureteral calculi*

| Authors                            | Lithotriaptor | n    | Stone free    | Retreatment  | Auxiliary procedures | Ureteral catheter |
|------------------------------------|---------------|------|---------------|--------------|----------------------|-------------------|
| <i>Proximal ureter</i>             |               |      |               |              |                      |                   |
| Tiselius <sup>207</sup> (1991)     | Dormer HM3    | 88   | 94% (83/88)   | 27% (24/88)  | –                    | 100% (88/88)      |
| Cass <sup>48</sup> (1992)          | Dornier HM3   | 386  | 77% (211/273) | 5% (19/386)  | 8% (21/273)          | 100% (273/273)    |
| Cass <sup>48</sup> (1992)          | Dormer HM3    | 478  | 73% (243/333) | 4% (18/478)  | 2% (5/333)           | 0% <sup>a</sup>   |
| Danuser et al <sup>47</sup> (1993) | Dornier HM3   | 46   | 96% (44/46)   | 2% (1/46)    | –                    | 0%                |
| Danuser et al <sup>47</sup> (1993) | Dormer HM3    | 48   | 94% (45/48)   | 0% (0/48)    | –                    | 0% <sup>a</sup>   |
| Subtotal                           | Dornier HM3   | 1046 | 79% (626/788) | 6% (62/1046) | 4% (26/606)          | 46% (361/788)     |
| Cass <sup>48</sup> (1992)          | Medstone STS  | 192  | 81% (101/124) | 6% (12/192)  | 7% (9/124)           | 100% (124/124)    |



|  |  |        |                     |                   |                         |                      |
|--|--|--------|---------------------|-------------------|-------------------------|----------------------|
| Cass <sup>48</sup> (1992)                      | Medstone STS                               | 218    | 73%<br>(93/127)     | 4% (9/218)        | 2% (2/127)              | 0% (0/127)           |
| Voce et al <sup>208</sup><br>(1993)            | MPL 9000                                   | 247    | 96%<br>(236/247)    | 20% (50/247)      | 5% (11/247)             | 9% (21/247)          |
| Chang et al <sup>209</sup><br>(1993)           | Lithostar                                  | 26     | 77% (20/26)         | 33% (8/26)        | 8% (2/26)               | 0% (0/26)            |
| Chang et al <sup>209</sup><br>(1993)           | Lithostar                                  | 27     | 59% (16/27)         | 26% (7/27)        | 22% (6/27)              | 100%<br>(27/27)      |
| Chang et al <sup>209</sup><br>(1993)           | Lithostar                                  | 24     | 63% (15/24)         | 23% (10/44)       | 21% (5/24)              | 100%<br>(24/24)      |
| Ilker et al <sup>210</sup><br>(1994)           | MLF 5000                                   | 85     | 84% (71/85)         | —                 | —                       | 0% (0/84)            |
| Frabboni et al <sup>211</sup><br>(1994)        | MPL 9000                                   | 247    | 96%<br>(236/247)    | 20% (50/247)      | 5% (11/247)             | 9% (21/247)          |
| Mobley et al <sup>55</sup><br>(1994)           | Siemens<br>Lithostar                       | 8477   | 85%<br>(4853/5719)  | 11%               | 5%                      | 24%<br>(1373/5719)   |
| Grasso et al <sup>212</sup><br>(1995)          | Lithostar                                  | 27     | 59% (16/27)         | 11% (3/27)        | 37% (10/27)             | 0% (0/27)            |
| Kupeli et al <sup>213</sup><br>(1998)          | Siemens<br>Lithostar                       | 458    | 61%<br>(279/458)    | —                 | —                       | 0% (0/458)           |
| Gnanapragasam et al <sup>214</sup><br>(1999)   | Dornier MFL<br>5000                        | 83     | 90% (84/93)         | —                 | 9% (8/93)               | 16% (15/93)          |
| Strohmaier et al <sup>215</sup><br>(1999)      | Modulith                                   | 38     | 76% (29/38)         | —                 | 24% (9/38)              | 39% (15/38)          |
| Coz et al <sup>21</sup> (2000)                 | Modulith SL-20                             | 397    | 84%<br>(226/268)    | 31%<br>(123/397)  | —                       | —                    |
| Subtotal                                       | 2nd and 3rd<br>generation<br>lithotriptors | 10,546 | 84%<br>(6275/7510)  | 19%<br>(272/1425) | 7% (73/980)             | 22%<br>(1620/7241)   |
| Authors  | Lithotriaptor                              | n      | Stone free          | Retreatment       | Auxiliary<br>procedures | Ureteral<br>catheter |
| <i>Middle ureter</i>                           |  |        |                     |                   |                         |                      |
| Tiselius <sup>207</sup> (1991)                 | Dornier HM3                                | 62     | 97% (59/61)         | 34% (21/61)       | —                       | 98% (60/61)          |
| Cass <sup>216</sup> (1994)                     | Dornier HM3                                | 33     | 75% (18/24)         | 6% (2/33)         | 13% (3/24)              | 91% (30/33)          |
| Cass <sup>216</sup> (1994) <sup>b</sup>        | Dornier HM3                                | 20     | 53% (9/17)          | 5% (1/20)         | 24% (4/17)              | 95% (19/20)          |
| Nakada et al <sup>217</sup><br>(1995)          | Dormer HM3                                 | 33     | 73% (19/26)         | 4% (1/26)         | 19% (5/26)              | 54% (14/26)          |
| Subtotal                                       | Dormer HM3                                 | 148    | 83%<br>(105/128)    | 18% (25/140)      | 18% (12/67)             | 88%<br>(123/140)     |
| el-Damounhoury, et al <sup>194</sup><br>(1991) | Siemens<br>Lithostar                       | 191    | 66%<br>(117/176)    | —                 | —                       | 66%<br>(126/191)     |
| Mobley et al <sup>198</sup><br>(1993)          | Siemens<br>Lithostar                       | 3077   | 83%<br>(1733/2,086) | 12%               | 7%                      | 25%<br>(769/3077)    |
| Cass <sup>216</sup> (1994)                     | Medstone STS                               | 101    | 80% (63/79)         | 6% (96/101)       | 8% (6/79)               | 88%<br>(89/101)      |
| Fujimoto et al <sup>218</sup><br>(1994)        | Dornier MFL<br>5000                        | 21     | 100% (16/16)        | 38% (8/21)        | 5% (1/21)               | 5% (1/21)            |
| Ehreth et al <sup>219</sup>                    | Dormer MFL                                 | 323    | 83%                 | 18% (58/323)      | 14% (41/299)            | 41%                  |

|  |  |      |                     |                  |                 |                    |
|--|--|------|---------------------|------------------|-----------------|--------------------|
| (1994)                                       | 5000                                       |      | (202/244)           |                  |                 | (134/323)          |
| Grasso et al <sup>212</sup><br>(1995)        | Siemens<br>Lithostar                       | 4    | 75% (3/4)           | 0% (0/4)         | 25% (1/4)       | 0%                 |
| Bierkens et al <sup>220</sup><br>(1998)      | Siemens<br>Lithostar                       | 19   | 90% (17/19)         | 53% (10/19)      | 11% (2/19)      | 0%                 |
| Park et al <sup>221</sup><br>(1998)          | MPL 9000                                   | 131  | 92%<br>(120/131)    | 11% (15/131)     | –               | 0%                 |
| Kupeli et al <sup>213</sup><br>(1998)        | Siemens<br>Lithostar                       | 396  | 51%<br>(204/396)    | –                | –               | 0%                 |
| Gnanapragasam et al <sup>214</sup><br>(1999) | MFL 5000                                   | 35   | 89% (31/36)<br>(36) | –                | 11% (4/36)      | 0%                 |
| Strohmaier et al <sup>215</sup><br>(1999)    | Modulith<br>Compact                        | 22   | 77% (17/22)         | –                | 23% (5/22)      | 41% (9/22)         |
| Subtotal                                     | 2nd and 3rd<br>generation<br>lithotriptors | 4320 | 79%<br>(2523/3209)  | 31%<br>(187/599) | 13% (60/480)    | 26%<br>(1128/4317) |
| <i>Distal ureter</i>                         |  |      |                     |                  |                 |                    |
| Erturk et al <sup>222</sup><br>(1993)        | Dormer HM3                                 | 312  | 81%<br>(199/245)    | 4.0%<br>(14/312) | 11%             | 79%                |
| Tiselius <sup>207</sup> (1991)               | Dornier HM3                                | 212  | 97%<br>(205/212)    | 23% (49/212)     | 7% (15/212)     | 62%                |
| Anderson et al <sup>49</sup><br>(1994)       | Dornier HM3                                | 27   | 96% (26/27)         | 3% (2/65)        | 6% (4/65)       | 0%                 |
| Turk and<br>Jenkins <sup>223</sup> (1999)    | Dornier HM3                                | 44   | 78% (35/44)         | –                | –               | –                  |
| Pearle et al <sup>224</sup><br>(2002)        | Dornier HM3                                | 32   | 100% (29/29)        | 0% (0/32)        | 0% (0/32)       | 16% (5/32)         |
| Subtotal                                     | Dornier HM3                                | 627  | 89%<br>(494/557)    | 10% (65/621)     | 6% (19/309)     | –                  |
| Chang et al <sup>209</sup> (1993)            | Lithostar                                  | 32   | 59% (19/32)         | 0% 0/32          | 41% (13/32)     | 0%                 |
| Voce et al <sup>208</sup> (1993)             | MPL 9000                                   | 285  | 97%<br>(276/285)    | 34%<br>(95/285)  | 3% (9/285)      | 4%                 |
| Anderson et al <sup>49</sup><br>(1994)       | Lithostar                                  | 22   | 84% (18/22)         | 14% (3/22)       | 14% (3/22)      | 18%                |
| Mobley et al <sup>198</sup><br>(1993)        | Siemens Lithostar                          | 7271 | 83%<br>(4084/4921)  | 10%              | 9%              | 13%                |
| Frabboni et al <sup>211</sup><br>(1994)      | MPL 9000                                   | 285  | 97%<br>(276/285)    | 17%<br>(49/285)  | 4% (12/285)     | 4%                 |
| Grasso et al <sup>212</sup><br>(1995)        | Lithostar                                  | 11   | 64% (7/11)          | 0% (0/11)        | 18% (2/11)      | –                  |
| Kupeli et al <sup>213</sup> (1998)           | Siemens Lithostar                          | 726  | 42%<br>(306/726)    | –                | –               | –                  |
| Park et al <sup>221</sup> (1998)             | MPL 9000                                   | 131  | 92%<br>(120/131)    | 11%<br>(15/131)  | –               | –                  |
| Eden et al <sup>225</sup> (1998)             | Modulith                                   | 313  | 75%<br>(235/313)    | –                | 26%<br>(81/313) | 16%                |
| Strohmaier et al <sup>215</sup><br>(1999)    | Modulith Compact                           | 37   | 59% (22/37)         | –                | 41% (15/37)     | 16%<br>(6/37)      |

|   |  |        |                    |                   |                   |    |
|---|--|--------|--------------------|-------------------|-------------------|----|
| Pardalidis et al <sup>226</sup><br>(1999) | Siemens Lithostar                          | 395    | 99%<br>(391/395)   | 6% (23/368)       | 1% (4/368)        | –  |
| Turk and Jenkins <sup>223</sup><br>(1999) | HM3/MFL 5000                               | 91     | 73%                | 15% (14/91)       | 7% (6/91)         | –  |
| Peschel et al <sup>227</sup><br>(1999)    | MFL 5000                                   | 40     | 90% (36/40)        | 0%                | 10% (10/40)       | –  |
| Gnanapragasam et al <sup>214</sup> (1999) | Dornier MFL 5000                           | 62     | 86% (53/62)        | –                 | 15% (6/92)        | 8% |
| Coz et al <sup>21</sup> (2000)            | Modulith SL-20                             | 639    | 91%<br>(406/446)   | 17%<br>(110/639)  | –                 | –  |
| Subtotal                                  | 2nd and 3rd<br>generation<br>lithotriptors | 10,340 | 81%<br>(6249/7706) | 17%<br>(309/1864) | 10%<br>(161/1576) | –  |

<sup>a</sup> Pushback SWL.

<sup>b</sup> Included only patients with multiple stones.

ureteroscopy for distal ureteral stones, many urologists are reluctant to treat distal stones with SWL. Nonetheless, mean stone-free rates of 89% (range 78–100%) for Dornier HM3 SWL and 81% (range 42–99%) for SWL with newer-generation lithotriptors have been achieved (see Table 27.6). Although no prospective randomized trials have compared outcomes for in-situ vs stent bypass SWL for distal ureteral stones, several series have reported stone-free rates exceeding 90% with in-situ SWL.<sup>49</sup>

## Special situations

### *Pediatric*

Although SWL is widely used in the pediatric population, concerns about the effects of shock waves on the developing kidney persist. Experimental studies in immature rats demonstrated long-term effects on renal function and permanent histologic damage. Likewise, Claro and colleagues found red cells in Bowman's space and glomerular congestion at 6 months in rats treated with SWL at 40 days of age.<sup>50</sup> Clinically, Lifshitz and coworkers found a significant decrease in renal growth in 29 children post-SWL followed for a median of 9 years, although it was unclear if the renal growth impairment was a consequence of SWL treatment or due to intrinsic pathology associated with the stonebearing pediatric kidney.<sup>51</sup> However, when compared with an untreated group of stone-bearing kidneys, the SWLtreated group demonstrated a significantly greater decrease in renal growth. In contrast, in a multi-institutional study from France, no impairment in renal function, assessed by immediate post-treatment renal scintigraphy, was demonstrated in 122 children treated with SWL on a variety of lithotriptors.<sup>52</sup> Likewise, Traxer and coworkers found no evidence of post-SWL renal parenchymal damage on DMSA scans in 39 children at a mean follow-up of 9 years.<sup>53</sup>

Although no clear-cut evidence links long-term renal functional impairment with SWL in the developing kidney, it is advisable to take measures to minimize potential tissue injury. In-vitro studies have shown that the minimum pressure level required to disintegrate urinary calculi is 200 bar and kidney damage occurs at pressures over 400

bar.<sup>55</sup> Consequently, successful tissue-protective treatment should be achievable in the pressure range of 200–400 bar.<sup>54</sup> While a narrow focal zone may also minimize the potential risk of renal damage,<sup>55</sup> the number of shock waves (in a range between 100 and 4000) does not appear to correlate with tissue damage.<sup>51</sup>

The overall success rates for SWL in children are high and the pediatric ureter seems to accommodate the passage of large volumes of stone fragments well. A number of pediatric series utilizing a variety of lithotriptors has yielded stone-free rates between 68 and 98% at 3-month follow-up with associated complication and retreatment rates of 2–20% and 9–28%, respectively.<sup>51,56–60</sup> Although pediatric SWL is highly successful, it is advisable to treat with the fewest shocks at the lowest power possible until further studies clarify the effect of shock waves on the pediatric kidney.

### *Transplant kidneys*

Stone localization for SWL in the transplant kidney can be challenging because of the location of the allograft in the bony pelvis, which limits fluoroscopic visualization and potentially causes attenuation of shock waves. Consequently, these patients are best treated with SWL in the prone position.<sup>45</sup>

There are relatively few and mostly small series in the literature of SWL treatment of renal calculi in transplant kidneys. The largest series involves 5 patients with 6 stones (1 ureteral and 5 calyceal), all less than 2 cm in size (mean 10.4 cm, range 7–15 cm), treated with a Wolf Piezolith 2500 lithotripter.<sup>61</sup> Although all patients were rendered stone free by a mean of 15 days after SWL, 1 patient required percutaneous nephrostomy drainage to relieve obstruction due to stone fragments. Long-term allograft function remained unchanged, with a mean serum creatinine level of 1.7 mg/dl before and 1.8 mg/dl after treatment. Additional anecdotal reports of SWL in allograft kidneys support the high success rates<sup>64</sup> and preservation of kidney function was reported by Klinger and colleagues.<sup>61</sup>

### *Horseshoe kidney*

The relative impairment of renal drainage due to the anteriorly located ureter as it crosses the isthmus, and the dependent, medially located calyces in the horseshoe kidney potentially compromise fragment clearance after SWL. Treatment of stones in horseshoe kidneys was first performed in the supine position on the Dornier HM3 lithotripter. Smith and colleagues were able to successfully target 14 of 16 stones in patients with horseshoe kidneys, but achieved only a 57% stone-free rate, including retreatments in 4 patients.<sup>64</sup> Locke and associates, also using the Dornier HM3 lithotripter and supine positioning, reported a 73% stone-free rate in 11 patients with horseshoe kidneys, including a 29% retreatment and 29% auxiliary procedure rate.<sup>65</sup> In an effort to improve stone targeting and treatment success, Jenkins and Gillenwater introduced a modified Stryker frame to allow for prone positioning.<sup>45</sup> In combined series of patients treated on the Dornier HM3 lithotripter in the supine and prone position, a stone-free rate of 62% was achieved, with retreatment and auxiliary procedure rates of 23% and 15%, respectively.<sup>64–68</sup> Newer-generation lithotriptors have been associated with comparable stone-free rates (67%), and retreatment and auxiliary rates of 38.1% and 8.5%, respectively.<sup>69–73</sup> Overall, the success

rates and retreatment rates for SWL in horseshoe kidneys are inferior to those achieved in anatomically normal kidneys.

#### *Pelvic kidney*

SWL treatment of stones in pelvic kidneys requires prone positioning in order to avoid impedance of the shock waves by the bony pelvis and the anteriorly located bowel. Using prone positioning on a Dornier HM3 or Wolf Piezolith lithotripter, Rigatti and associates achieved a 92% stone-free rate in 12 patients, although retreatment was necessary in 43% of patients.<sup>74</sup>

#### *Solitary kidney*

The indications for SWL treatment of stones in a solitary kidney are the same as for patients with two kidneys. However, precautions must be taken to avoid postoperative renal obstruction from stone fragments or a decline in renal function. Success rates for SWL treatment of stones in solitary kidneys range from 62 to 88% at 3–12 months postSWL. Zanetti and coworkers achieved a stone-free rate of 62% at 12–24 months post-treatment in 37 solitary kidneys with >2 cm stones; however, 3 patients developed obstruction and azotemia, necessitating drainage with a stent or nephrostomy tube.<sup>75</sup> Kulb and associates performed SWL using a Dornier HM3 lithotripter in 68 patients with solitary kidneys and achieved a stone-free state in 64%.<sup>18</sup> Complications included obstruction in 6 patients and 2 perirenal hematomas necessitating blood transfusion. Sarica and colleagues treated 22 patients (36 stones) with solitary kidneys using SWL. Among 14 patients with 3-month follow-up, 64% were rendered stone free. Ureteral stents were placed preoperatively in all patients and there were no cases of obstruction following treatment.<sup>76</sup>

Although in most series, the placement of a ureteral stent prior to SWL was reserved only for cases of obstruction, this practice will result in post-SWL obstruction in 6–17% of patients. Consequently, the routine placement of a ureteral stent may be advisable, although placement based on stone size cannot be determined from the literature.

#### *Obesity*

Poor fluoroscopic and ultrasound visualization of the stone, weight limitations on the table, and a skin-to-stone distance that may exceed the distance between F1 and F2 limit SWL treatment of stones in obese patients. Stone localization and treatment may be improved by using the extended shock wave pathway (blast path) with or without abdominal compression.<sup>77</sup> In a series of 81 morbidly obese patients, mean weight 326 lbs (148 kg), treated on a Medstone STS lithotripter using these modifications, a stone-free rate of 78% was achieved at 3 months.<sup>78</sup>

#### *Synchronous bilateral shock wave lithotripsy*

After isolated case reports of bilateral ureteral obstruction and acute renal failure following synchronous bilateral SWL, it was generally recommended that bilateral renal

calculi be treated with SWL in a staged fashion.<sup>79</sup> However, two recent large series suggest that synchronous bilateral treatment may be safe in a select patient population.

Pienkny and Stroom reviewed their series of 360 patients with bilateral renal calculi treated with SWL on the Dornier HM3 lithotripter either simultaneously ( $n=319$ ) or staged ( $n=41$ ).<sup>80</sup> Although the two groups in this retrospective series differed in age, pretreatment serum creatinine, stone burden, and number of shocks administered, there was no significant difference between the two groups in the change in serum creatinine from baseline to a mean of 3.5 years post-SWL. Furthermore, retreatment (8.9%) and complication rates (8.9%) in the simultaneous bilateral treatment group were comparable to those reported in the literature for unilateral SWL treatment.

Perry and colleagues also retrospectively evaluated the records of 120 patients who underwent simultaneous bilateral SWL with the Dornier HM3 lithotripter and reported a bilateral stone-free rate of 60% after a single treatment. Complications occurred in 15% of patients, all of which were minor, and no patient developed bilateral ureteral obstruction or renal failure. Of note, there was no change in serum creatinine after treatment.<sup>81</sup>

### **Maneuvers to improve stone fragmentation and stone passage**

Stone fragmentation during SWL has been shown to be dependent on the rate of shock wave delivery. With the first-generation Dornier HM3 lithotripter, shock waves were synchronized with the electrocardiogram, and shock wave rate rarely exceeded 60–80 shocks per minute. However, with newer, ungated lithotriptors, shock wave delivery rate has been increased in order to reduce treatment times. Several recent in-vitro studies, however, have shown that stone fragmentation is enhanced by slowing the shock wave rate to less than 120 shock waves per minute.<sup>82–84</sup> Indeed, Paterson and colleagues recently showed in an in-vivo porcine model that stone fragmentation was more efficient with SWL treatment at 30 shocks per minute than with 120 shocks per minute.<sup>85</sup> The clinical utility of this finding remains to be confirmed, but this study represents a first step toward optimizing SWL treatment parameters.

Several investigators have described mechanical maneuvers for improving fragment clearance after SWL. D'a Honey and associates evaluated the use of inverted patient positioning in combination with percussion therapy and forced diuresis to improve passage of stone fragments, particularly following SWL for lower pole calculi. Among 12 patients with <2 mm residual fragments 2 weeks after SWL treatment of lower pole calculi who were treated with mechanical percussion and inversion therapy (MPI) preceded by 20 mg of furosemide, immediate post-MPI radiographs demonstrated movement of stone fragments out of the lower pole in 11 patients, with complete clearance of fragments in 8 patients.<sup>86</sup> Indeed, 4 patients passed stones in their first voided urine post-MPI, and 10 patients passed fragments during the 2-week follow-up period. Based on the success of this pilot study, MPI was prospectively compared to observation in a group of 69 patients with <4 mm residual lower calyceal stone fragments at 3 months post-SWL.<sup>87</sup> The stone-free rate associated with MPI was significantly higher than the control group (40% vs 3%, respectively).

Other investigators have recommended adjuvant medication regimens aimed at decreasing ureteral inflammation, reducing ureteral spasm, and enhancing urinary flow to facilitate discharge of fragments after SWL. The combination of a calcium channel blocker (to reduce ureteral spasm without affecting peristaltic activity) and a corticosteroid (to diminish ureteral edema) has been shown to improve spontaneous ureteral stone passage and reduce episodes of renal colic.<sup>88,89</sup> Porpiglia and associates prospectively compared a regimen of nifedipine and deflazacort vs no adjuvant treatment for enhancing fragment clearance after SWL. Among 80 patients undergoing SWL treatment on the Sonolith 4000+ lithotripter, 75% of study patients compared with 50% of control patients were noted to have completely expelled stone fragments by 45 days post-treatment.<sup>90</sup> Furthermore, the treatment group required significantly less pain medication compared with the control group. Side-effects from the nifedipine and deflazacort were seen in only 10% of the patients, none of whom discontinued the medications.

Azm and Higazy prospectively evaluated the utility of forced diuresis on the clearance of fragments after SWL of ureteral calculi.<sup>91</sup> A total of 106 patients with ureteral calculi were randomized to SWL with or without the intravenous administration of 500 ml of normal saline containing 40 mg furosemide. A marginally higher fragmentation and stone-free rate was achieved in the diuretic group compared with the control group at 3 months, a difference most pronounced for stones in the distal ureter. The authors speculated that diuresis creates a fluid interphase between the ureteral wall and stone that could account for improved fragmentation and enhanced stone passage.

Soygur and colleagues evaluated the efficacy of potassium citrate in preventing stone recurrence and facilitating discharge of residual fragments after SWL in 110 patients with lower pole calcium oxalate stones.<sup>92</sup> Patients rendered stone free or left with <4 mm residual fragments were randomized to receive potassium citrate (60 mEq daily) or no treatment 4 weeks after SWL. Among 56 stone-free patients, the stone recurrence rate was 0% and 28.5%, respectively, for potassium citrate-treated vs control patients, respectively. Among the 34 patients with residual fragments, potassium citrate-treated patients showed resolution of their residual fragments in 44.5% compared with only 12.5% of control patients.

The use of adjuvant mechanical maneuvers and medical regimens to facilitate discharge of fragments after SWL may improve stone-free rates and allow lower pole stones in particular to be successfully treated with SWL. Although most of these regimens were initiated a few weeks after SWL treatment, the institution of these measures immediately post-procedure may further enhance stone-free rates and speed the rate of clearance of fragments.

### **Contraindications to shock wave lithotripsy**

Contraindications to SWL therapy have changed over time as our experience with lithotripsy and understanding of the physics and biology of the process has expanded. Currently, the only absolute contraindications to SWL treatment are untreated bleeding diathesis and pregnancy.

*Untreated bleeding diathesis*

Blood dyscrasias predispose the kidney to SWL-induced perinephric and subcapsular hematomas, and consequently, hematologic abnormalities should be corrected prior to SWL.<sup>93</sup> Likewise, medications that affect the coagulation cascade (heparin, warfarin) or platelet function (aspirin, NSAIDs) should be discontinued at an appropriate time prior to SWL to allow clotting mechanisms to normalize. If hematologic parameters cannot be corrected prior to treatment, the patient should be rescheduled for an alternate therapy such as ureteroscopy, which has been shown to be safe and effective in patients with known and uncorrected bleeding diatheses.<sup>94</sup>

*Pregnancy*

Pregnancy remains an absolute contraindication to SWL because of the unknown effect of shock waves on the developing fetus. A study in pregnant rabbits showed that SWL produced congestion and focal parenchymal microhemorrhages in the lung, liver, and kidneys of fetuses exposed to shock waves early in gestation.<sup>95</sup> In another study, rat fetuses located near the focal zone (F2) had lower birth weights after SWL treatment than control, untreated fetuses.<sup>96</sup> However, despite these animal data demonstrating deleterious effects of shock waves on the developing fetus, there have been several reports of pregnant women unwittingly undergoing SWL during the first trimester without adverse sequelae. Asgari and coworkers reported on 6 females not known to be pregnant who underwent ultrasound-guided SWL for renal stones during the first month of pregnancy; all women gave birth to healthy babies with no evidence of chromosomal abnormalities or birth defects.<sup>97</sup>

Frankenschmidt and Sommerkamp performed the only reported case of intentional SWL during a known pregnancy in a woman with an obstructing proximal ureteral calculus who failed conservative management and refused percutaneous nephrostomy tube placement.<sup>98</sup> Shock wave lithotripsy was performed at 5 weeks gestation using the Piezolith 2300 lithotripter because of its a small focal zone (6×10 mm) and ultrasound-based imaging. The fetus, located 11 cm from the stone, was monitored during the procedure with ultrasound and cardiotocography. Treatment proceeded uneventfully, the stone was successfully fragmented, and the patient had an uncomplicated postoperative course, ultimately delivering a healthy, fullterm baby of normal size and weight. At 6 years post-SWL no adverse sequelae to mother or child have been reported.

Despite the lack of documented adverse clinical outcomes from SWL during pregnancy, pregnancy must still be considered an absolute contraindication to SWL treatment and alternative forms of therapy should be pursued for management of stones during pregnancy.

*Aneurysm*

Aortic and renal aneurysms were previously considered relative contraindications to SWL because of concern for potential aneurysm rupture. Although there have been a few reports of aneurysm rupture following SWL, there is increasing evidence that SWL can be performed safely in select patients with aneurysms providing appropriate precautions are taken.<sup>99,100</sup> Carey and Streem recommended limiting SWL treatment to patients with



aneurysms <5 cm in size in whom the distance between the aneurysm and stone exceeds 5 cm.<sup>101</sup> Deliveliotis and colleagues recommended close monitoring during treatment of patients with aneurysms, and suggested that only renal and not ureteral stones be treated, using low-voltage and minimal shocks.<sup>102</sup> In an in-vitro study by Vasavada and coworkers, calcified aortic aneurysmal tissue harvested from patients undergoing elective abdominal aneurysm repair was exposed to shock waves of varying energies and distances from Fl.<sup>103</sup> No significant difference in histopathologic findings was found between control and calcified tissue exposed to shock waves.

In the first clinical report of SWL treatment of a stone in a patient with an untreated abdominal aortic aneurysm, Thomas and associates reported no adverse event.<sup>104</sup> Likewise, Deliveliotis and colleagues reported on a series of 5 patients with abdominal aortic aneurysms and symptomatic stones treated with SWL in whom all but 1 patient was successfully treated and no patient experienced an adverse event.<sup>102</sup>

### *Cardiac pacemaker*

Early versions of the first-generation lithotripter were associated with cardiac arrhythmias in 80% of patients treated. As such, lithotriptors were subsequently triggered to deliver shock waves only during the refractory period of the ventricular cardiac cycle by gating the shock wave to the R wave of the patient's electrocardiogram (ECG).<sup>105</sup> However, newer-generation lithotriptors were again ungated in an effort to improve stone fragmentation and decrease treatment times. Ganem and Carson showed that ungated SWL treatments on the Medstone STS lithotripter were associated with a greater number of arrhythmias than gated treatments, although the arrhythmias that occurred were uniformly benign and resolved readily when treatment was converted to ECG-gating.<sup>106</sup> Flam and coworkers treated 25 patients with a Sonolith 4000+ lithotripter and randomly alternated periods of gating and ungating to observe cardiac effects.<sup>107</sup> During the ungated period, ventricular and supraventricular rhythm disturbances were noted in 7 patients, although in no case was the arrhythmia associated with hemodynamic instability; on the other hand, no arrhythmias occurred during the gated periods.

The safety of treating patients with pacemakers or implanted cardiac defibrillators with SWL has been questioned due to potential malfunction from electromagnetic inference or the possibility of damage to the device from the physical force of the shock. However, Cooper and associates analyzed the response of pacemakers exposed to shock waves in vitro and found that single chamber pacemakers performed normally during SWL.<sup>108</sup> On the other hand, shock wave treatment occasionally induced inhibition of ventricular output in dual chamber pacemakers, and therefore these investigators concluded that patients with single-chamber pacemakers or dual-chamber devices reprogrammed to the WI or DDD mode can be treated safely with SWL. Abber and colleagues also studied pacemaker function in vitro during SWL and found that shock waves delivered synchronously with pacemaker spikes resulted in abnormal pacemaker function in only 1 of 22 cases; in contrast, shock waves discharged at a rate faster than the set rate of the pacemaker caused malfunction in half the devices.<sup>109</sup> Consequently, to protect against malfunction, they recommended that a cardiologist and a temporary pacemaker be available during treatment and that two-chamber sensing pacemakers should be reprogrammed to a one-chamber sensing mode.

The clinical safety of SWL treatment of patients with pacemakers was evaluated by Drach and coworkers, who surveyed 196 lithotripsy centers in the United States and Europe to determine the incidence of pacemaker-related complications during SWL.<sup>110</sup> Among 142 SWL treatments in 130 pacemaker patients, 3 minor complications and only 1 serious complication occurred (in a patient in whom spontaneous deprogramming of a programmable pacemaker occurred that was rapidly corrected by the attending cardiologist without incident). The authors concluded that pacemakers do not pose undue risk during SWL treatment provided that the patient has been evaluated and cleared by his cardiologist, the type of pacemaker is well-documented, and a temporary pacemaker as well as an experienced cardiologist is available during treatment.

Unlike pacemakers that are usually implanted at a site remote from the kidney, cardioverter defibrillators are typically implanted subcutaneously in the abdomen. Nonetheless, patients with implantable cardioverter defibrillators may be treated safely with SWL if the stonebearing kidney is contralateral to the defibrillator, the defibrillator is set to inactive mode, and the posterior thorax is shielded with styrofoam.<sup>111–113</sup> However, it is prudent to consult a cardiologist for evaluation of the device before, as well as after, treatment.

## Complications

The complications of shock wave lithotripsy can be divided into obstructive problems related to stone passage and direct tissue injury to the kidney.

### *Steinstrasse*

Obstruction associated with passage of stone fragments often occurs transiently and resolves spontaneously. Occasionally, however, a column of stone fragments may accumulate in the ureter ('steinstrasse') when a leading fragment becomes impacted and obstructs the passage of subsequent fragments or when gravel forms sludge that becomes lodged in the ureter. Steinstrasse have been reported to occur in 6–20% of patients after SWL, with an incidence that varies directly with stone size.<sup>114–118</sup> Kim and associates reported an incidence of Steinstrasse of only 0.3% after SWL treatment of stones less than 1 cm in size, but a 10% and 17% incidence of Steinstrasse for stones between 2 and 3 cm and 3 and 4 cm, respectively.<sup>115</sup> Likewise, Sayed and colleagues reported an incidence of Steinstrasse among 885 patients treated on a Dornier MPL 9000 lithotripter of 0.3%, 7.1%, and 11.5% for stones <1 cm, 1–2 cm, and 2–3 cm, respectively.<sup>117</sup>

Although preoperative stent placement may prevent obstruction associated with Steinstrasse, it probably does not prevent Steinstrasse from occurring. In a series of 650 SWL treatments, Weinerth and colleagues reported Steinstrasse formation in 19 patients, among whom 47% had a ureteral stent and 11% had a nephrostomy tube in place at the time of treatment.<sup>116</sup> Among the patients with Steinstrasse and a ureteral stent, two-thirds showed no evidence of obstruction. In contrast, Sulaiman and coworkers found a significantly higher incidence of Steinstrasse among unstented patients (38%) compared with stented patients (15%) for those treated for stones >2 cm in size.<sup>119</sup> The incidence of

Steinstrasse in patients with stones <2 cm in size, however, did not differ significantly between stented and unstented groups.

Madbouly and colleagues evaluated the effect of stone, patient, and treatment characteristics on Steinstrasse formation associated with SWL in an effort to identify predictive factors of occurrence.<sup>118</sup> Among 4634 patients treated with a Dornier MFL 5000 lithotripter over a 10-year period, Steinstrasse developed in 184 patients (4%), 74 of whom required intervention. The incidence of Steinstrasse correlated significantly with stone size and location, the presence of hydronephrosis, and the power level used during treatment. Renal stones were associated with an almost 3-fold greater incidence of Steinstrasse compared with proximal ureteral stones, and stones >2 cm in size were nearly 4 times more likely to result in Steinstrasse than smaller stones. Hydronephrosis was associated with a 1.8 times greater risk of Steinstrasse formation, which was attributed to decreased renal pelvic and ureteral peristalsis. Lastly, power greater than 22 kV was associated with a higher risk of Steinstrasse formation.

Approximately two-thirds of steinstrasse will resolve spontaneously. For those that fail to resolve, placement of a percutaneous nephrostomy tube often facilitates passage of stone fragments by restoring ureteral peristalsis. If the fragments still fail to clear with renal drainage, treatment with repeat SWL to a leading fragment or ureteroscopic or percutaneous treatment should constitute definitive treatment. In the case of infection associated with obstruction from a column of fragments, urgent decompression of the collecting system with nephrostomy drainage is mandated prior to definitive stone management.

### *Renal hematoma*

The incidence of clinically significant post-SWL renal hematomas is less than 1% in reported series.<sup>120,121</sup> However, CT or MRI (magnetic resonance imaging) detects renal hematomas in 15–30% of cases.<sup>122–124</sup> Risk factors for the development of perinephric hematomas include untreated coagulopathic conditions, hypertension, obesity, pre-existing urinary tract infection, and bilateral treatment.<sup>121,125,126</sup> The mechanism of hematoma production has been ascribed to shock wave cavitation-induced injury to the vascular wall.<sup>126</sup> Atherosclerotic plaques decrease the elastic properties of blood vessels and may make them more susceptible to SWL-related complications in hypertensive individuals. Surprisingly, stone size, the number of sessions, the number of shock waves, and the energy applied have not been shown to correlate with hematoma formation.

The vast majority of symptomatic patients are successfully treated with conservative therapy consisting of analgesics and bed rest. Transfusion or angiographic/operative intervention is rarely necessary, and occurs almost exclusively in the face of coagulative disorders.<sup>127</sup> Spontaneous hematoma resolution has been noted in 64–85% of cases at 1–2 years.<sup>128</sup> Krishnamurthi and Streem found no increased incidence of hypertension or decreased renal function in patients with post-SWL hematomas.<sup>128</sup>

### **Bioeffects of shock wave lithotripsy**

Lingeman and coworkers were the first to intensively investigate the tissue and biological effects of Shockwave lithotripsy.<sup>129</sup> Now, 20 years later, we are only beginning to understand the consequences of shock wave application to renal tissue and how to minimize the deleterious effects. Moreover, as the technology of newer-generation lithotriptors evolves, these bioeffects will change as well.

#### *Renal function*

Although Chaussy and associates observed no change or an improvement in renal function in humans and dogs following SWL, there is strong evidence that SWL causes parenchymal damage to the kidney in the acute setting. The proposed mechanism of damage is a decrease in renal plasma flow (RPF) and/or glomerular filtration rate (GFR) as a result of SWL-induced vascular injury and subsequent renal vasoconstriction.<sup>51,130–132</sup>

Several investigators evaluated the role of shock wave treatment parameters on the production of histologic renal lesions in an animal model.<sup>133–135</sup> Shock wave kilovoltage and peak pressure correlated most strongly with the size of the renal lesion. No direct correlation between shock wave number and lesion size was seen, but significant renal lesions were found to occur only at relatively high numbers of shock waves (>4500). Tubular damage, as measured by urine levels of N-acetyl D-glucosaminidase, however, did strongly correlate with shock wave number and intensity.<sup>136</sup> Of note, the contralateral unshocked kidney was also found to undergo an acute decrease in RPF, most likely as a result of either activation of renal sympathetic nerves or release of systemic vasoconstrictors from the treated kidney.<sup>137</sup>

There is conflicting evidence regarding the eventual sequelae of these acute renal tissue effects. Wilson and colleagues examined the effects of four different surgical treatment modalities for renal calculi (piezoelectric SWL, pyelotomy, nephrotomy, and percutaneous nephrostomy tube with balloon dilation) on renal function and morphology in a porcine model.<sup>138</sup> None of the treatment modalities demonstrated a significant change in creatinine clearance or effective RPF at 1-month post-treatment compared to pretreatment values. Also, histologic analysis of the SWL-treated kidneys 1 month following treatment demonstrated renal scarring in less than 0.1% of the renal parenchyma. The absence of chronic renal injury has been confirmed in other human studies that showed no change in renal function following SWL.

#### *Hypertension*

There have long been concerns that SWL may be associated with the long-term development of hypertension. Although most retrospective studies have found no association between SWL and the development of new onset hypertension,<sup>139,140</sup> Lingeman and colleagues reported a slight, but significant rise in diastolic blood pressure (0.78 mmHg) post-treatment.<sup>141</sup> The proposed mechanism for SWL-induced hypertension involves the 'Page kidney effect' in which the renal parenchyma is compressed by

fibrosis resulting from perirenal hematoma formation, thereby reducing renal blood flow and stimulating release of renin and angiotensin II. Indeed, a reduction in renal blood flow has been confirmed in an animal model,<sup>142</sup> and later demonstrated in humans by Janetschek and associates who found durable changes in renal resistive indices in patients exposed to SWL.<sup>143</sup>

The effect of SWL on the development of hypertension has been evaluated in two prospective randomized trials. Jewett and coworkers randomized 154 normotensive patients with renal calculi to SWL treatment or observation and obtained baseline and follow-up blood pressure measurements in all patients.<sup>144</sup> At a mean follow-up of 1 year, no significant difference between the two groups in the observed incidence of new onset hypertension was found (2.7% in the SWL group vs 2.5% in the observation group). Likewise, Elves and colleagues randomized 228 patients (normotensive and hypertensive) with renal calculi to SWL or observation.<sup>145</sup> At a mean follow-up of 2.2 years, 7% of subjects in the control group and 11% in the SWL group were newly diagnosed with hypertension ( $p=0.35$ ). Furthermore, in this series no relationship was found between the number of shock waves delivered and the development of hypertension.

On the other hand, Knapp and colleagues measured resistive index (RI) in both kidneys before and after SWL in 76 patients and noted a significant increase in RI (from 0.6203 to 0.6717) in the treated kidneys but no change from baseline in the untreated kidneys.<sup>146</sup> The mean age of patients who experienced an increase in RI was 66 years old, and a linear positive correlation was noted between post-SWL RI and patient age. Further study of 57 patients from this same group at a mean of 26 months posttreatment demonstrated a continued significant increase in RI from baseline and a 17.5% incidence of new-onset hypertension. Of note, 45% of patients older than 60 years of age developed new-onset hypertension within 26 months of SWL. With 1 exception, an increase in RI and new-onset hypertension were seen only in patients >60 years of age. Consequently, patients over 60 years of age may be at risk for disturbances of renal perfusion and 45% may develop new-onset hypertension within 26 months of SWL. Although there is no conclusive proof that SWL results in an increased incidence of hypertension in the general patient population, older patients may represent a subpopulation at higher risk for new-onset hypertension after SWL.

### *Genital organs*

Because of the potential deleterious effect on the ovary from SWL treatment of stones in the middle or distal ureter, SWL is not recommended for women of childbearing age. However, no animal studies have clearly demonstrated injury to the ovaries in association with SWL. Recker and colleagues treated 28 female rats with 600–1200 shock waves and found minor subcapsular bleeding and cellular damage to the ovaries in 2 of 14 acute animals and no long-term damage in a chronic group of animals.<sup>147</sup> Similarly, McCullough and colleagues found no evidence of deleterious effects of shock waves on rat ovarian follicles with 1500 shock waves at 20 kV.<sup>148</sup>

In a retrospective review of 84 woman of childbearing age treated with SWL, Vieweg and colleagues found no increased incidence of infertility, miscarriages, or fetal abnormalities.<sup>149</sup> Likewise, Erturk and associates surveyed 39 women of childbearing age

who underwent SWL for distal ureteral calculi, and found that among 10 women who attempted to become pregnant, no infertility problems were encountered and 11 healthy babies were delivered.<sup>150</sup> Although these studies appear to support the safety of SWL in women of childbearing age, prospective studies will probably never be performed and SWL treatment of middle and distal ureteral calculi should still be avoided in women of childbearing age.

There have also been theoretical concerns about the effects of SWL on male fertility. In an in-vitro study by Huwe and colleagues, human spermatozoal suspensions were treated with 3000 shocks at increasing distances from the shock wave focal point.<sup>151</sup> Significant impairment of spermatozoal motility parameters occurred within 3 cm of F2, although at further distances from the focal zone no change in sperm motility was detected. Andreessen and associates also demonstrated a significant decrease in sperm density and motility when sperm were exposed to SWL in vitro.<sup>152</sup> Likewise, these parameters were also decreased from baseline in vivo in men treated with SWL for distal calculi, although the differences were not significant at 3 months after treatment. Transient hemospermia occurred in 30% of patients after SWL, probably due to the close proximity of the ureter to the seminal vesicles. It appears that the effects of SWL on male fertility are transient and most probably mediated by the proximity of the ureter to the seminal vesicles rather than a direct testicular effect.

#### *Effects on other tissues*

Because of the difference in acoustic density between water and air, the air-filled lungs are susceptible to SWL-induced injury, especially in the pediatric patient, where the lungs are in close proximity to the targeted stone. Application of a layer of Styrofoam around the chest wall has been shown to protect the lungs by absorbing the shock wave energy. Other air-filled structures such as the gastrointestinal tract have rarely been a site of SWL-induced trauma. Colonic mucosal ecchymoses have led to guaiac-positive stools in up to 4% of patients undergoing SWL.<sup>153</sup> Likewise, there have been two case reports of small bowel perforations following SWL, although this is an extremely unlikely complication.<sup>154,155</sup>

### **Nonrenal shock wave lithotripsy applications**

#### *Peyronie's disease*

In an effort to find an effective, noninvasive treatment for Peyronie's disease, Butz and Teichert applied shock wave technology to the management of Peyronie's plaques.<sup>156</sup> Using a flexible-arm lithotripter (Stortz Minilith or Siemens Lithostar overhead) with in-line ultrasonography and palpation of the plaque for localization, investigators have reported alleviation of pain in 56–100% of patients, a decrease in penile deviation in 25–68%, and a perceived improvement in sexual intercourse in 43–62%.<sup>157–159</sup>

Lebret and coworkers first described the use of a standard lithotripter (Multiline Siemens lithotripter) for shock wave treatment of Peyronie's disease.<sup>160</sup> In 54 patients, Peyronie's plaques were localized fluoroscopically after injection of the plaques with

iodinated contrast, and then treated one or more times with 3000 shock waves (7 kJ) per session applied to the flaccid penis using minimal sedation. Improvement in penile angulation was noted in 54% of patients, and in 61% of patients an overall subjective improvement was reported post-treatment. Among 35 patients with painful erections preoperatively, 91% reported a decrease in pain after treatment. Few self-limiting complications (7 buttock petechiae, 3 penile hematomas, and 1 case of urethral bleeding) were reported. The long-term efficacy of SWL for Peyronie's disease has not yet been established, but it appears to be a safe and effective minimally invasive treatment option for this difficult-to-treat disease.

### *Salivary calculi*

Sialolithiasis is the most common disease of the major salivary glands, with 80% of salivary gland calculi located in the submandibular glands, 10% in the sublingual glands, and 10% in the parotid glands.<sup>161</sup> There are no effective chemolytic agents for salivary gland calculi, and conservative treatment has met with mixed success. Dilatation of the salivary ducts is successful only in cases of small, distally located calculi. Consequently, surgical extirpation of salivary gland calculi has constituted the treatment of choice, despite a limited risk of facial nerve injury. In an effort to treat sialolithiasis in a less-invasive manner, Iro and coworkers first applied shock waves to the stone bearing salivary gland using a piezoelectric lithotripter.<sup>162</sup> Since then, SWL has commonly been used as salvage therapy after conservative treatment fails. Success rates, defined as stone free on post-treatment imaging, have ranged from 50 to 81%<sup>163,164</sup> with the highest stone-free rates observed for the subgroups of patients with parotid gland calculi, stones less than 1 cm, and stones located near the hilum of the gland.<sup>165</sup> The morbidity associated with SWL of salivary gland calculi has been limited to skin surface petechiae, gland swelling, and blood-tinged salivary secretions. In limited series, glandular function appears to be preserved following SWL therapy.<sup>166</sup>

### *Cholelithiasis*

SWL was first used for the treatment of gallstones in Germany in 1986 using the ultrasound-based, second-generation Dornier MPL 9000.<sup>167</sup> The success rate of SWL treatment for cholelithiasis depends on adequate stone fragmentation, which in turn determines clearance rates.<sup>168</sup> Animal studies have shown that fragments larger than 5 mm are unable to transverse the cystic duct.<sup>169</sup>

A review of 10 series, comprising 2761 patients undergoing SWL treatment of gallstones, revealed that some degree of fragmentation occurred in 95.7% of patients although only 48% of patients achieved adequate fragmentation after the initial treatment.<sup>170</sup> In a pooled analysis of 13 studies comprising 1101 patients, the fragment-free rate at 1 year was 58%, with the best results obtained in patients with single stones less than 20 mm in size.

Oral litholytic agents were originally used as an adjunct to SWL therapy to improve stone clearance. However, there are conflicting results on the routine use of bile acids post-SWL.<sup>171</sup> Tsumita and associates observed complete disappearance of gallstones in 74% (193 of 262) of patients treated with SWL, without the use of adjuvant litholytic

agents.<sup>172</sup> However, recurrence occurred in 50 (26%) of the 193 patients at mean follow-up of  $2.6 \pm 2.1$  years. The cumulative incidence of stone recurrence following SWL treatment at 3, 5, and 7 years was 21%, 27%, and 33%, respectively. However, ursodeoxycholic acid was shown to be effective in clearing stones in patients with gallstone recurrences, and for decreasing the incidence of biliary colic following SWL treatment.

Relatively few adverse events have been reported with gallstone lithotripsy. Although intramural hematomas and edema of the gallbladder wall are common, rupture of the gallbladder has not been reported.<sup>173</sup> The most significant complication involves obstruction of the cystic or common bile duct during passage of stone fragments. In a review of 11 series, comprising over 2000 patients, the frequency of these complications was as follows: biliary colic, 45.5%; need for cholecystectomy due to acute cholecystitis or intolerable pain, 2.8%; need for endoscopic sphincterotomy for biliary duct obstruction, 0.8%; and pancreatitis, 1.4%.<sup>174</sup>

### *Pancreatic calculi*

Sauerbruch and colleagues first reported on the use of SWL to treat pancreatic duct calculi in 1987.<sup>175</sup> Since then, SWL has been advocated as an adjunct to endoscopic retrograde cholangiopancreatography (ERCP) and sphincterotomy and as an alternative to open surgery when ERCP alone fails in the treatment of pancreatic duct calculi. The first series from the United States was reported by Wolf and associates at Washington University, St. Louis, in 1995.<sup>176</sup> In this series 12 patients underwent 14 SWL treatments for pancreatic duct calculi to relieve obstruction and assist in the endoscopic management of chronic pancreatitis. Using a Dornier HM3 lithotripter, stones were localized fluoroscopically with or without the use of injected iodinated contrast via a nasobiliary tube to opacify the pancreatic duct and then treated with a mean of 2000 shocks at 20 kV, after which the fragments were extracted by ERCP. Adequate stone fragmentation was achieved in 13 of 14 treatments, and post-SWL ERCP resulted in complete or partial extraction of fragments in 7 and 4 cases, respectively. Of note, no complications occurred and no patients developed post-SWL pancreatitis. Complete or partial symptomatic relief was attained in 4 cases each at a mean follow-up of 19–22 months.

Although SWL of pancreatic calculi may adequately fragment stones, endoscopic retrieval is generally required for extraction of fragments. However, Ohara and colleagues treated 32 patients with SWL alone and achieved a stone-free rate of 75% and relief of pain in 79% at a mean follow-up of 44 months.<sup>177</sup> No serious complications occurred and pancreatic exocrine function improved in 61% of patients. Thus, SWL therapy, with or without endoscopic fragment retrieval, should be considered for pancreatic calculi that fail endoscopic means alone.

### *Plantar fasciitis*

SWL has been used since the early 1990s for the treatment of a variety of musculoskeletal disorders. In October 2000 the United States Food and Drug Administration (FDA) approved an electrohydraulic lithotripter (Dornier Med Tech EPOS Ultra) for use in the treatment of chronic proximal plantar fasciitis. A number of



placebo-controlled trials have since demonstrated a beneficial effect of SWL therapy for this disorder.<sup>178–180</sup> However, Buchbinder and colleagues randomized 160 patients with ultrasoundproven plantar fasciitis to either an active SWL treatment group or a sham control group and found no difference between the two groups with regard to pain or quality of life at 6 and 12 weeks post-SWL treatment.<sup>181</sup> Further studies are clearly needed to establish the benefit, if any, of SWL treatment for this indication.

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# Shock wave physics of lithotripsy: mechanisms of shock wave action and progress toward improved shock wave lithotripsy

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## Introduction

Shock wave lithotripsy (SWL) for the treatment of urinary stones was introduced to clinical practice in the early 1980s. Today, even with the refinement of endourologic methods for stone removal such as ureteroscopy and percutaneous nephrolithotomy, SWL remains the primary treatment for uncomplicated upper urinary tract calculi.<sup>1</sup> Although considered to be highly successful, lithotripsy is plagued by the occurrence of adverse effects and increased rates of significant injury linked to the use of high acoustic output machines. Clinical experience and studies with experimental animals treated with the first lithotripter—the Dornier HM3—have shown that a dose of shock waves sufficient to comminute a stone invariably causes trauma to the kidney.<sup>2-4</sup> This injury can be severe and can lead to longterm complications such as new-onset hypertension.<sup>5</sup> In addition, recent studies now show that the present generation of ‘high-pressure’ lithotriptors produce low stone-free rates, high retreatment rates, and an increased incidence of adverse effects.<sup>6-21</sup> Thus, a technology that should be the best treatment option has become more problematic and the lithotripter has become a risk factor in SWL.

This chapter:

1. reviews the design characteristics of current and emerging lithotriptors and correlates these features with stone comminution and tissue injury
2. outlines current understanding of the mechanisms of stone breakage by shock waves
3. describes the factors that contribute to tissue injury in SWL
4. recommends a strategy based on current understanding of lithotriptors and mechanisms of shock wave action to improve SWL.

## Lithotripter design and performance

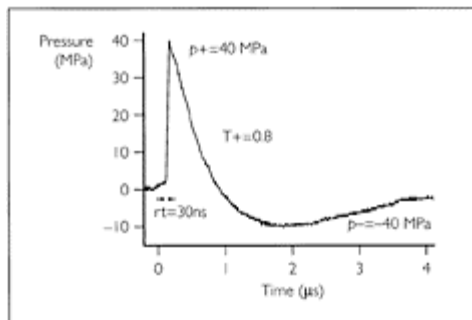
### *Present status of clinical lithotriptors*

Lithotriptors have evolved considerably since the 1980s when the first clinical lithotripter, the unmodified Dornier HM3, was introduced. This machine was an electrohydraulic spark-gap device in which the patient (under sedation) rested in a water bath. The Dornier HM3 lithotripter has proven to be highly successful, and remains today the gold standard in SWL. Since the introduction of the Dornier HM3 lithotripter, more than 40 different lithotriptors have been used to treat patients. Each machine may have its unique features (mostly incidental differences), but all have three main components in common:

- a shock wave source
- a coupling medium to transmit the shock pulse to the body
- an imaging system for targeting the stone.

Among the various lithotriptors, there are few fundamental differences in any of these components.

A representative focal waveform generated by the unmodified Dornier HM3 lithotripter is shown in Figure 28.1. The pulse consists of a compressive phase with a peak amplitude of  $\sim 40$  MPa and duration  $\sim 1$   $\mu$ s, followed by a tensile tail with peak amplitude  $\sim -10$  MPa and duration  $\sim 3$   $\mu$ s. The pulse leads with a shock wave of  $\sim 10$  ns rise time (measured in water). However, this measurement is affected by the limited bandwidth ( $<100$  MHz) of



**Figure 28.1** A typical shock wave at the focus of an unmodified Dornier HM3 lithotripter. The pulse consists of a compressive phase followed by a tensile tail.

available hydrophones, and the Taylor shock thickness for a shock of these amplitudes is of the order 0.1 ns. The waveform measured in vivo is very similar to that shown in Figure 28.1, except that the rise time is lengthened to ~70 ns.<sup>22</sup>

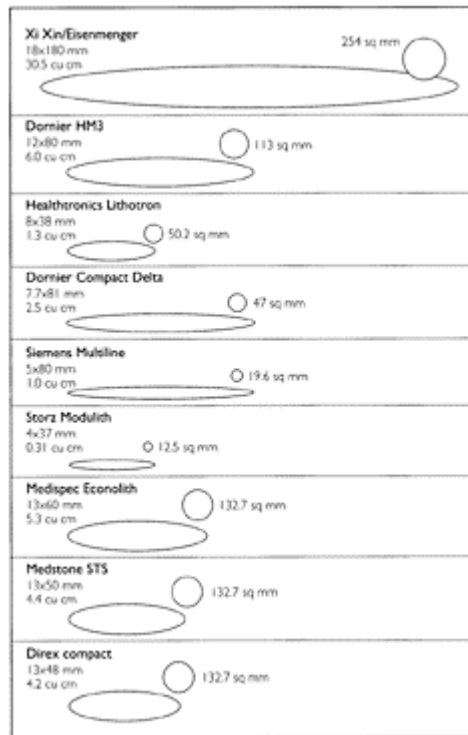
Lithotripsy shock waves are generated by one of three mechanisms: electrohydraulic spark discharge; electromagnetic deflection of a plate; and piezoelectric transduction. The vast majority of clinical devices are either electrohydraulic or electromagnetic. The shock pulse is focused to a cigar-shaped region that, depending on the lithotripter design, is ~3–18 mm wide and ~35–180 mm long (Figure 28.2). Electrohydraulic lithotriptors typically have a larger focal zone than electromagnetic or piezoelectric lithotriptors.

The evolution of lithotripter design over the years has occurred in several rather poorly defined phases. The original first-generation lithotripter, the Dornier HM3—although it was very effective—had two features that to some seemed in serious need of improvement:

1. shock wave coupling required immersion in a water bath
2. it was necessary to place the patient under sedation.

The water bath was mostly an inconvenience and this problem was solved by enclosing the shock head in a water-filled chamber capped with a latex membrane that could be coupled to the body with ultrasound gel. Although there is no better way to transmit shock waves to the body than by immersing the patient in water, all but a few lithotriptors now use a gel coupling system.

Making lithotripsy anesthesia-free proved to be a bigger issue: not because it was a harder problem to solve, but because the solution required modification of the shock wave source, and this, over time, has led to subsequent



**Figure 28.2** The shape of the focal (oval) area and cross-sectional diameter (circle to the right) for each of the 9 lithotriptors listed in Figure 28.3 is shown.

modifications that have made lithotriptors more dangerous and less effective. Patient discomfort during shock wave treatment is primarily due to the perception of pain over the area of shock wave entry into the body. The engineering solution for this was to use a wider aperture at the shock wave source so that the acoustic energy was spread over a broader area of skin. Thus, second-generation lithotriptors were designed to be anesthesia-free. This was an attractive selling point for the lithotripsy industry and the most competitive of the manufacturers developed anesthesia-free machines. The competition was keen and inspired other improvements at about the same time. Thus, the typical second-generation lithotripter used 'dry table' coupling, was constructed as modular components for portability, and many were designed as multifunctional endourologic workstations. Unfortunately, this translates as too many 'advances' too soon, and, for the most part, anesthesia-free lithotriptors were not very effective.

The response from the lithotripter industry was to develop machines that were more powerful—to break stones better—but, they were intended to be used anesthesia-free.

Apparently to compensate for the limited effectiveness of second-generation machines, third-generation lithotriptors used shock waves with extremely high amplitudes—two- to three-fold higher than the Dornier HM3 lithotripter (Figures 28.2 and 28.3). Like their predecessors, these third-generation lithotriptors used a broad aperture. A broad aperture spreads the area of contact of the acoustic pulse with the body, but this also narrows and shortens the zone of high pressure at the shock wave focus (see Figure 28.2). The tighter the focal zone, the harder it is to keep on target. If the patient is not under sedation, this not only makes it more difficult to hit the stone but also increases the likelihood of shock waves being delivered to renal tissue.

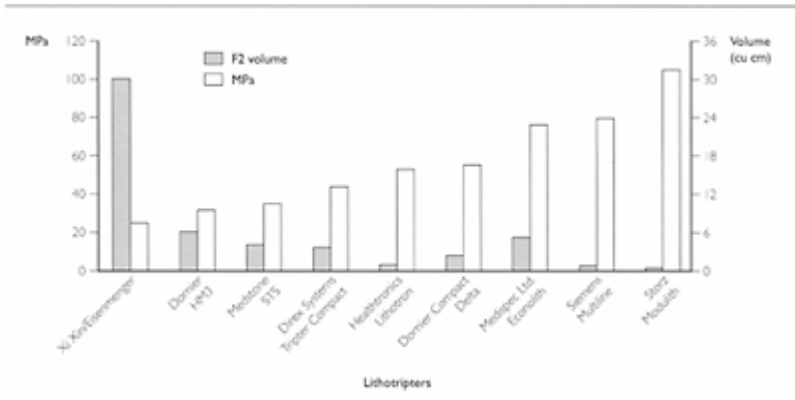
These powerful, tight-focal-zone, third-generation lithotriptors have proven to be problematic and are characterized by lower stone-free rates,<sup>6,9</sup> higher retreatment rates,<sup>10</sup> and an increased occurrence of adverse effects (e.g. subcapsular hematomas, colon perforations, and ruptured spleens)<sup>11–16</sup> than occurs with the Dornier HM3 lithotripter. These studies report hematoma rates from 3 to 12%, rates much higher than the 0.6% rate reported for the unmodified Dornier HM3 lithotripter.<sup>17–21</sup> The stone-free rate can be improved for these machines if the patient is anesthetized, suggesting that a reduction in body movements permits more direct hits of the shock wave on the stone.<sup>9</sup> Thus, the engineering advances that characterize the newer-generation machines have not improved outcomes for patients and, indeed, these new lithotriptors are both less effective in breaking stones and more traumatic to renal tissue.

### *Emerging lithotripter designs*

If 'high-pressure, tight-focal zone' lithotriptors (third-generation lithotriptors) are indeed less effective than the original HM3 technology, perhaps lithotripsy needs to be reinvented. A step in this direction has been taken with the recent introduction of the Xi Xin-Eisenmenger lithotripter.<sup>23</sup> This wide-focus, low-pressure lithotripter is an electromagnetic device that generates a pressure field of 10–25 MPa with a focal zone of 18×180 mm (see Figures 28.2 and 28.3). The initial clinical report based on data from 297 patients suggests that no anesthesia is necessary and the stone-free rate is very good (86%) after a 3-month follow-up.

All currently available commercial lithotriptors use a single-shock source. Of great interest are several recent reports of experimental lithotriptors that employ dualshock wave sources.<sup>24–30</sup> The rationale for twin-head lithotripsy comes from the pioneering work of Bailey<sup>24</sup> and colleagues<sup>26</sup> who have demonstrated that dual pulses fired simultaneously and head-on dramatically alter cavitation activity at F2, thereby providing a means of controlling cavitation. Similar results have been reported by Sheir





**Figure 28.3** The peak amplitude vs size of the focal volume of 9 different lithotriptors are compared. The trend (left to right) that has occurred in lithotripsy design to increase the peak pressure while decreasing the size of the focal area is illustrated.

et al.<sup>28</sup> Other investigators<sup>25,27</sup> have fired dual pulses along the same axis in an attempt to suppress tissue damage and enhance stone comminution. All of these studies suggest that stone breakage is enhanced by dual-pulse treatment, but no published studies have as yet reported the effect of dual pulses on tissue injury. Auge et al.<sup>30</sup> have reported in an abstract, and Sheir and Clayman<sup>29</sup> in a presentation, that tissue injury is reduced with dual pulses. These data are intriguing and suggest that twin-head lithotripsy may improve the safety and effectiveness of SWL. It must be realized that the action of a dual-source lithotripter in breaking stones is likely to be more complex than that of a conventional lithotripter; the design of any such device may influence mechanisms of shock wave interaction and their effectiveness at breaking stones, but also the potential for tissue injury. Thus, there is need for experiments to obtain objectively determined data on this new concept in lithotripsy before twin-head, dual-pulse technology enters into clinical use.

## Mechanisms of stone comminution

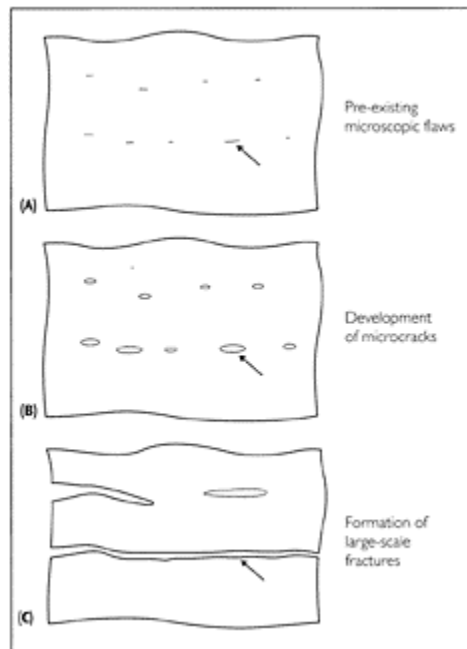
### *Physical factors*

The precise events involved in stone comminution have yet to be determined, but there is good evidence to show that multiple mechanisms are at play. At least four potential mechanisms for SWL stone breakage have been described:

1. compression fracture
2. spallation
3. squeezing
4. acoustic cavitation.

Failure by compression fracture is dependent on the large positive pressure generated by the shock wave. As the compressive front passes through the stone (front to back) it generates a stress distribution, with both compressive and shear components, that will result in material failure, particularly in the vicinity of pre-existing defects in the stone such as grain boundaries, cavities, inclusions and cracks (Figure 28.4).<sup>31</sup>

Kidney stones may break by a process involving spallation, also known as the Hopkinson effect (Figure 28.5A), in which the compressive wave is reflected at sites of acoustic impedance mismatch, in particular, at the distal surface of the stone (stone-fluid interface) and is inverted in phase to a tensile (negative pressure) wave. Most brittle materials (such as kidney stones) are much weaker in tension than in compression. Thus, the magnitude of the tensile wave is more likely to exceed the tensile strength of the stone than is the incident compressive wave. Spallation is affected by

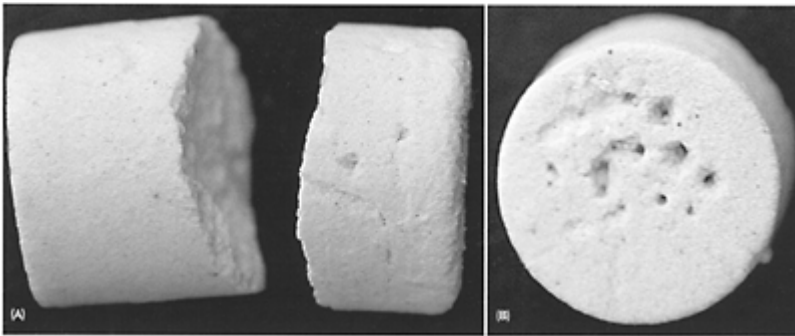


**Figure 28.4** The comminution of stones by shock waves is a progressive process where pre-existing sites of microflaws (arrow, A) grow and coalesce to form microcracks (B)

under the influence of a repetitive pulse of acoustic energy. These sites of microcracks (arrow) will continue to grow to form large-scale failure, resulting in fracture (C) and eventually fragmentation. This progressive process of stone failure is termed dynamic fatigue.

the size and the shape of the stone<sup>32</sup> and its material properties.<sup>33</sup> Stones that are more spherical in shape tend to focus the reflected tensile wave, further increasing the tensile stress. Spallation requires a finite distance for reflection and focusing of the shock wave: thus, if a stone, or the fragments of a stone, are too small, spall will not occur.<sup>34–36</sup>

Eisenmenger<sup>37</sup> has suggested an alternative mechanism for stone breakage in which the stone splits in the plane parallel to the direction of shock wave propagation failure due to circumferential squeezing. This mechanism of failure appears to be operable when the target stone is smaller than the diameter of the high-pressure zone of the lithotripter pulse. In studies using the ‘wide-focal zone, low-pressure’ lithotripter, artificial stones fragmented at very low pulse pressure (11 MPa). This is a potentially critical observation in light of the current trend in lithotripter design to greatly increase the pulse pressure while reducing



**Figure 28.5** Gypsum artificial stones showing damage characteristics of two mechanisms of shock wave action. (A) A stone is broken into two pieces—a damage pattern typical of failure by spallation. In this case the direction of shock wave propagation was from left to right. By this mechanism the incident compressive wave reflects off

the back of the stone, inverts in phase, and the stone fails in tension. (B) The leading face of a stone demonstrates pitting characteristics of surface erosion due to cavitation bubble collapse.

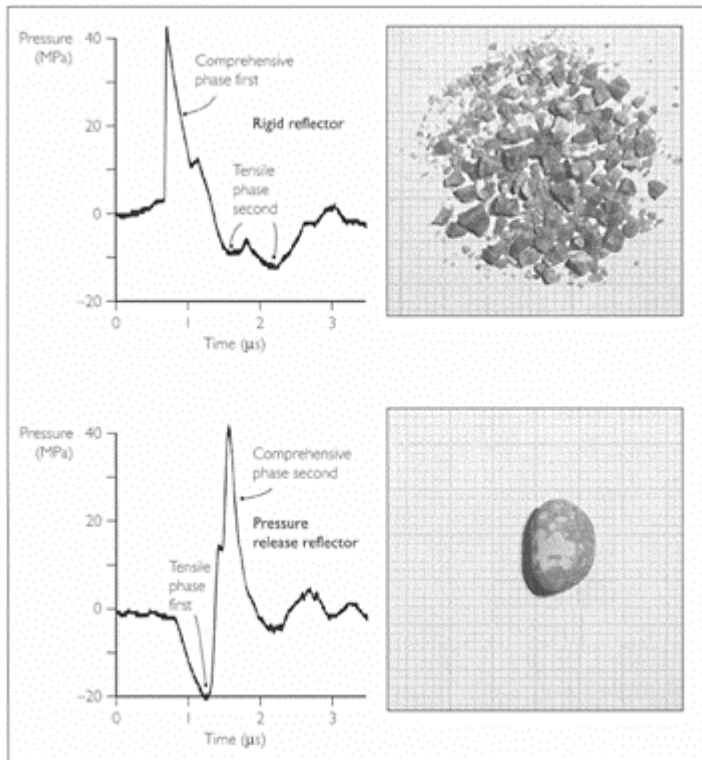
the size of the focal zone. Numerous studies have shown that cavitation bubble activity contributes to stone comminution.<sup>38–45</sup> Cavitation is a collective term that includes the formation and dynamic behavior (growth and collapse) of bubbles. In lithotripsy, bubbles grow in response to the tensile (negative-pressure trough) of the shock pulse. The amplitude of the negative pressure is so large ( $\sim$ 10 to  $\sim$ 20 MPa) as to cause water to fail in tension.<sup>46</sup> Fluids typically contain minute impurities that serve as nucleation points for bubble formation. Bubbles form from these cavitation nuclei, grow rapidly, and collapse violently. Cavitation bubbles can remain spherical during collapse, and release energy primarily by sound radiation in the form of a shock wave. This shock wave generates a positive and negative wave and, theoretically, is capable of inducing all of the fragmentation mechanisms described above. However, if the bubble collapses in the vicinity of a solid object, the collapse is asymmetric, generating a liquid jet (cavitation microjet).<sup>39</sup> Typical bubble radii in SWL vary from 1  $\mu$ m to 1 mm, and bubble jet velocities range from 22 m/s to 800 m/s. If the liquid jet is near the surface of a stone, it sets up a local compressive stress field in the stone, propagating spherically into the stone interior.<sup>43,44</sup>

Cavitation bubbles pit and erode surfaces<sup>47</sup> and the damage to stones caused by focal bubble collapse is distinct from damage due to failure mechanisms such as spall (Figure 28.5B). To determine if cavitation is the primary mechanism of stone fragmentation, investigators have developed in-vitro systems to minimize or eliminate cavitation. These systems include the use of viscous media in which cavitation is unlikely to occur<sup>41,48</sup> or the application of overpressure to suppress the growth of bubbles.<sup>49,50</sup> Both in-vitro systems have shown reduced stone damage with a reduction in cavitation activity alone.

Recent work by Bailey et al<sup>51, 52</sup> in which the order of the positive and negative waves of the pressure pulse were inverted using a pressure release reflector (PRel reflector) also showed a reduction in stone comminution (Figure 28.6). These studies showed the lifetime (bubble duration) of cavitation bubbles with the PRel reflector to be 50 times shorter, and the amplitude of the calculated acoustic emission of the collapsing bubbles to be 13 times smaller than with the standard rigid reflector. Also, cavitation pits in target foils treated with PRel reflector shock waves were measured to be 8 times smaller than with the rigid reflector: i.e. cavitation bubbles with the PRel reflector did not grow as large and they collapsed with less force than the cavitation bubbles that were generated with the rigid reflector. All of these studies suggest that SWL-induced cavitation has an enormous potential for producing damage in SWL.

The comminution of stones by shock waves is a progressive process. Stones are not reduced to sand instantaneously. Instead, they break gradually. Kidney stones in SWL probably fail by the same process understood to characterize the failure of any brittle solid, a process known as dynamic fatigue<sup>31</sup>—the growth and coalescence of minute

flaws within the stone (see Figure 28.4). Because renal stones are not homogeneous but have either a lamellar crystalline structure bonded by an organic matrix material or are agglomerates of crystalline and noncrystalline



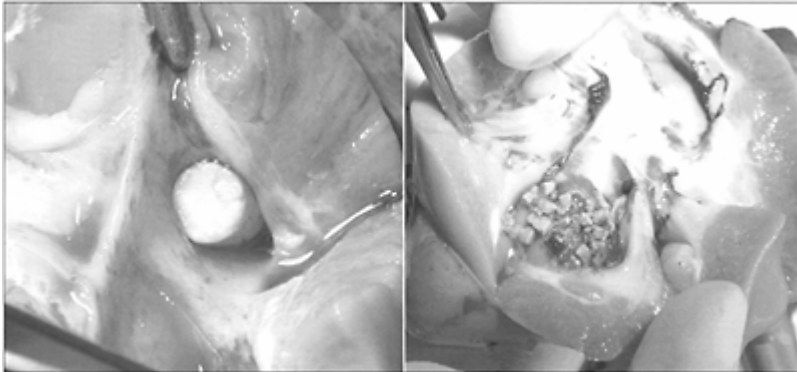
**Figure 28.6** The upper set of illustrations shows a typical lithotripsy shock wave and the degree of breakage caused by treatment of a human kidney stone (calcium oxalate monohydrate) with 75 shock waves using the Dornier HM3 lithotripter. The lower set of illustrations shows the inverted waveform generated by the pressure release reflector (PRel reflector). Treatment of a human kidney stone with 75 shock waves from the PRel reflector resulted in no breakage.

material, they have numerous pre-existing flaws. Shock wave treatment—repetitive pulses of acoustic energy progressively weakens the stone at these sites, resulting in the formation and growth of microcracks. The growth of microcracks leads to large-scale failure, which results in fracture and eventually fragmentation. All the mechanisms detailed for stone breakage probably involve this process of dynamic fatigue.

#### *Effects of treatment parameters on stone breakage*

Treatment parameters that can be selected by the urologist include the number of shock waves administered, the rate at which shock waves are delivered (pulse repetition rate), and the power setting of the lithotripter.

The rate of shock wave administration has been shown to influence stone breakage. Our group has explored the influence of rate on stone comminution using a new animal model.<sup>53</sup> The data from these studies clearly show that slowing the rate of shock wave delivery from 120 SW/min to 30 SW/min increases the fragmentation of artificial stones (Figure 28.7). A recent abstract has presented the first double-blind clinical trial to compare shock wave frequencies of 60 and 120 Hz,<sup>54</sup> and their interim analysis suggests that the slower rate is more effective. There is strong evidence to suggest that rapid delivery of shock waves promotes cavitation activity. In studies with animals, renal injury was increased by treatment at very fast rates.<sup>55</sup> Also, at fast rates bubbles along the acoustic



**Figure 28.7** The effect of shock wave rate on stone comminution: the effect of 30 SW/min (left panel) vs 120 SW/min (right panel) on artificial stones implanted into the collection system of a pig kidney. Each stone was treated with 400 shock waves at 20 kV in an unmodified Dornier HM3 lithotripter.

axis interfere with delivery of energy into the stone. Thus, fast rates may increase cellular damage and lower the efficiency of stone fragmentation. These data are of particular concern in that it is now common for the urologist to apply shocks as an ungated procedure, meaning the rate of shock wave delivery is not linked to heart rate. Newer lithotriptors allow shock wave administration at rates of 120–240 SW/min, a level that probably increases the risk of tissue damage and reduces stone fragmentation. These issues need clinical investigation.

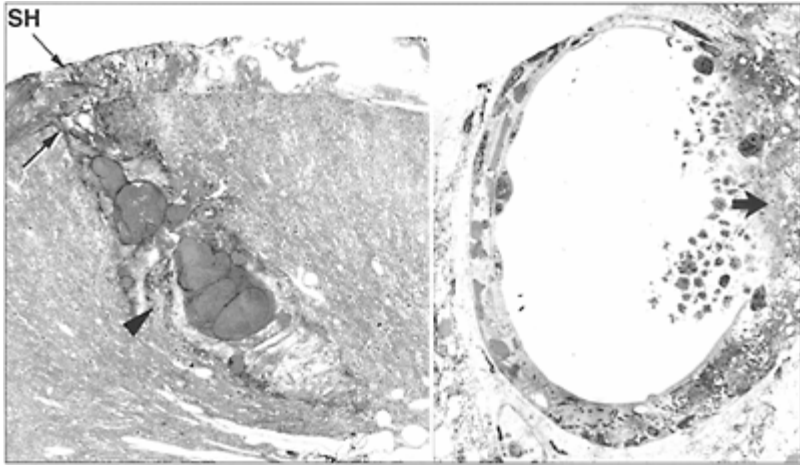
Shock wave pressure also appears to be a critical factor in lithotripsy, although the relationship of this factor to stone fragmentation may not be simple. Many newer lithotriptors have been designed to yield very high peak positive pressures ( $>100$  MPa), apparently under the assumption that bigger is better. However, early experience at the Methodist Hospital with the unmodified Dornier HM3 lithotripter suggested that stone fragmentation was equally good at settings of 12 or 24 kV (which corresponds to pressures of about 30–50 MPa).<sup>56</sup> This indicates that peak positive pressure may have less of a positive effect on stone fragmentation than might be expected. Similarly, the lower pressures of the Dornier HM3 lithotripter, compared to many newer machines, might be assessed to result in less efficient stone fragmentation. However, recent clinical data suggesting success with a very low pressure lithotripter<sup>23</sup> also speaks against the idea that 'more is better' with regard to shock wave pressures. Furthermore, higher incidences of adverse side-effects linked to the more powerful third-generation machines seem to show that higher shock wave pressures not only do not break stones better but also that high-amplitude shock waves increase patient risk. Thus, it seems that shock wave pressure is a critical factor in lithotripsy, but that the effectiveness of a lithotripter does not depend on this factor alone, and, indeed, higher-pressure shock waves can be counterproductive in SWL.

### **Mechanisms of tissue injury in shock wave lithotripsy**

Two main mechanisms have been suggested to explain the occurrence of tissue damage in SWL:

1. cavitation (defined here as SW-bubble interactions involving either the collapse or expansion of cavitation bubbles)
2. noncavitation forces such as a shear stress.

There is ample evidence that lithotripter shock waves generate cavitation in aqueous media<sup>38</sup> and that cavitation can occur within blood.<sup>57</sup> It is also true that renal injury in SWL is primarily a vascular lesion (Figure 28.8)<sup>58</sup> accompanied by a reduction in renal blood flow due to an SWL-induced vasoconstrictive response.<sup>59</sup> As such, it seems likely, even probable, that cavitation within blood vessels may be responsible for SW-induced hemorrhage.<sup>60</sup> One approach to confirming this relationship is to localize cavitation within kidney tissue and to precisely correlate the



**Figure 28.8** The left panel shows a large hemorrhagic site in a juvenile pig kidney treated with 2000 shock waves at 24 kV with an unmodified Dornier HM3 lithotripter. A lesion is seen extending from the corticomedullary junction to the renal capsule, resulting in a subcapsular hematoma (SH). A small island (arrowhead) of normal-appearing tubules is seen surrounded by this lesion. The right panel shows a severely injured small artery, as seen by transmission electron microscopy. Note the destruction of all smooth muscle cells and a thrombus plug at the site of the laceration (arrow).

site of tissue damage with bubble activity. This, however, is a nontrivial correlation. The resolution of existing cavitation detection methods is not fine enough to isolate individual renal vessels. Indeed, with conventional tools, such as ultrasound imaging and single transducer passive cavitation detection transducers, it is difficult to be certain of localization even within the functional tissue of the kidney. Thus, reports of cavitation bubble activity in the kidney without confirmatory localization by another method (to rule out bubble activity in the renal collecting system or perinephric fluid) have been encouraging, but only strongly suggestive of cavitation in the vicinity of renal tissue.

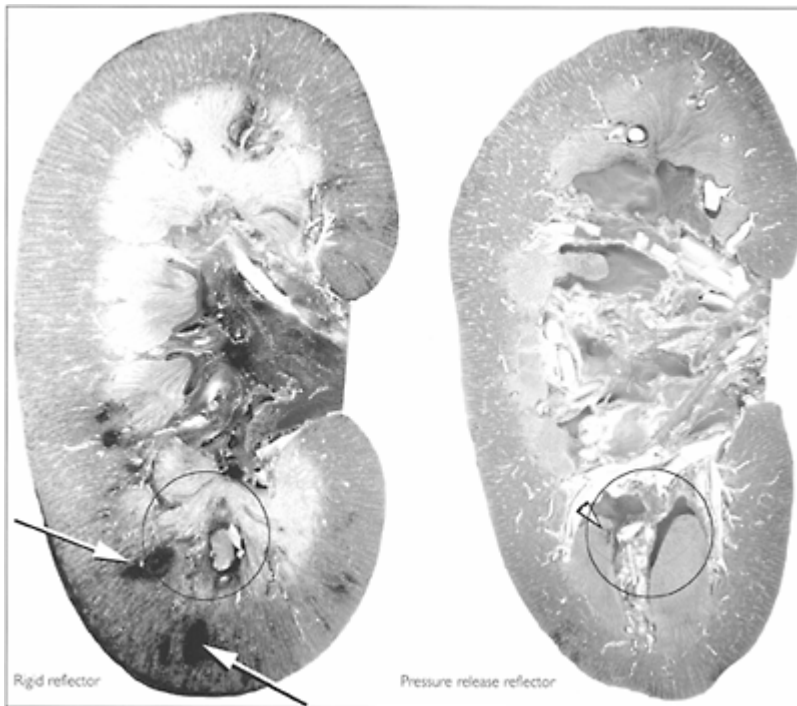
Recently, we have published a report in which lithotripter-induced cavitation was localized to the renal parenchyma.<sup>61</sup> In this work, a passive cavitation detection (PCD)



system using two confocal spherical-bowl PZT transducers was used for coincidence detection of cavitation bubble emissions within a  $2 \times 2 \times 2$  mm sampling volume centered at F2 of a Dornier HM3 lithotripter. An ultrasound scan head targeted at this spot was used to image echogenicity in and around the sample volume. Fluoroscopy and ultrasound were used to position the renal collecting system and then the renal parenchyma at F2. Signal (PCD emissions, hyperechoic spots) was intense from the urine space, but also present when F2 was focused on tissue. To further confirm the anatomic localization of the cavitation site, the PCD transducers were used as high-intensity focused ultrasound (HIFU) sources. Targeting was confirmed using HIFU below the lesion threshold to produce an echogenic spot detectable by ultrasound. Subsequently, an HIFU tissue lesion was created that marked the kidney parenchyma. Thus, it can be concluded that lithotripter shock waves produce cavitation within kidney tissue as well as within the urine space of the renal collecting system.

To further test the hypothesis that cavitation is the primary mechanism of tissue injury, we compared the degree of injury induced in the pig kidney following treatment with a clinical dose of shock waves with a standard rigid reflector vs the PRel reflector (see description above).<sup>61</sup> Pig kidneys treated with shock waves from a standard rigid reflector showed damage that was evident even on gross inspection as a subcapsular bleed consistently at the treated pole (lower pole) of the kidney but frequently extended to portions of the upper pole as well. Histologic analysis of the renal parenchyma showed a focal hemorrhagic lesion that involved both the cortex and medulla and commonly spanned the entire width of the kidney.<sup>59,62,63</sup> This zone of damage was focal, in that the parenchyma of the upper pole was never involved and there were broad areas of the treated, lower pole that appeared undamaged (Figure 28.9). In comparison, very little damage occurred to kidneys treated with the PRel reflector (see Figure 28.9).<sup>63</sup> These kidneys did not develop hematomas. On histologic analysis, the renal cortex was virtually undamaged and evidence of injury was limited to slight intraparenchymal bleeding in renal papillae (see Figure 28.9, arrowhead on right panel) that fell within the F2 focal zone of the lithotripter. Although such regions of bleeding were visible in histologic sections, these areas of hemorrhage were too slight to register by morphometric analysis. Based on our previous studies showing that the PRel reflector greatly suppresses cavitation *in vitro*,<sup>24</sup> we believe the renal injury induced with the standard rigid reflector is caused by cavitation.

So it is that lithotripter-induced cavitation can be localized to the renal parenchyma, and this strongly implicates cavitation in SWL renal trauma. However, it has been shown by numerical modeling<sup>31</sup> and by experiment<sup>64,65</sup> that lithotripter shock pulses have the potential to cause cell lysis by noncavitational mechanisms such as shear.



**Figure 28.9** The left panel shows the extensive amount of injury (arrows) induced by 2000 shock waves at 24 kV administered by a rigid reflector. The right panel shows a pig kidney treated with 2000 shock waves at 24 kV but with the PRel reflector. This kidney shows a limited amount of damage located within a renal papilla (arrowhead). The circles mark the location of F2 to the lower pole.

When vials of red blood cells (RBCs) were treated with shock waves, cell lysis with the PRel reflector was significantly lower than when the rigid reflector was used. This suggests that cavitation was responsible for most of the cell lysis that occurred with the rigid reflector.

In order to separate damage to isolated cells caused by cavitation from cell lysis due to noncavitational forces we used overpressure (OP) to suppress cavitation.<sup>49,50,64,66</sup> In theory, OP in excess of the amplitude of the tensile phase of the lithotripter pulse should prevent bubble growth and, thereby, prevent cavitation from occurring. In actuality,

cavitation in the free field can be suppressed by relatively low (~3–5 atm) excess hydrostatic pressure.<sup>49,66</sup> To make certain that cavitation would be eliminated, we exposed isolated RBCs to shock waves in an OP chamber capable of achieving >120 atm excess static pressure. The chamber was constructed with acoustic windows that had minimal effect on the waveform characteristics or amplitude of the pressure pulse.<sup>50</sup> Vials of RBCs placed in the chamber were exposed to shock waves at atmospheric pressure or at >120 atm OP. Lysis of cells treated with shock waves at OP was significantly lower than cell lysis when shock waves were administered at atmospheric pressure. This hemolysis at OP sufficient to preclude cavitation was still significantly higher than cell lysis in untreated (but pressurized) controls, which suggests that whereas most of the shock wave cell lysis was due to cavitation, significant cell damage occurred by a mechanism other than cavitation. This noncavitation damage was dependent on the kilovoltage of the shock source, with lysis significantly higher at 24 kV than at 16 kV and 20 kV.

Isolated RBCs *in vitro* are relatively large targets. With a diameter in fluid suspension of 7–9  $\mu\text{m}$ , RBCs approximate the size of circulating cells in the blood vasculature and in some tissue structures such as the walls of capillaries and small veins. Our *in-vitro* studies with OP showed (above) that significant shock wave damage was due to forces other than cavitation. Numerical modeling of shock wave propagation through a tissue-like medium predicts that the stress upon a target object is related to the size of the object.<sup>31,65,67</sup> Thus, larger targets should be under greater stress than smaller targets, but the size limit for target damage is difficult to estimate. In order to determine if lithotripter shock waves might be capable of causing damage to biological targets smaller than isolated cells, we conducted shock wave exposure experiments on phospholipid membrane vesicles similar in size (~100–150 nm) to intracellular organelles. Vesicles were more difficult to break than isolated cells. The lysis rate of vesicles was approximately 0.03% per 100 shock waves compared to 2.3% per 100 shock waves for isolated RBCs. To determine whether shock wave lysis of vesicles was dependent on cavitation, vials of vesicles were placed in the OP chamber and exposed to shock waves at atmospheric pressure or at ~130 atm OP. Vesicle lysis at OP was not different from lysis at atmospheric pressure, which indicates that shock wave damage to membrane vesicles was not due to cavitation: i.e. biological targets the size of intracellular organelles can be damaged by lithotripter shock waves, but by a mechanism that does not involve cavitation.

Overall, the results of these studies using biological targets as diverse as whole animals, isolated cells, and membrane vesicles suggest that lithotripter shock waves cause damage to tissue by more than one mechanism. Cavitation appears to be the dominant mechanism, but other forces appear to be at play as well. These studies also point to the value of approaching the problem of shock wave injury at different levels: i.e. with models that have different levels of biological complexity. The data show that our understanding of how shock waves injure the kidney is helped by use of simpler models, which may in themselves seem far from tissue. For example, cells in suspension lack the structural organization of tissues, so this simple system is not a particularly compelling model of a complex organ such as the kidney. However, with isolated cells it is possible to rigidly control the environment during shock wave exposure and this proves to be an important advantage. For example, isolated cells can be exposed to shock waves while at

high OP, a manipulation that is not feasible with a living animal. Use of this strategy to control cavitation has shown convincingly that cavitation is the dominant mechanism responsible for cell injury in vitro, but that shock wave-induced cell lysis is not due to cavitation alone.<sup>64,65</sup>

The idea that lithotripter shock waves may cause tissue damage by mechanisms other than cavitation has been suggested by others. Lokhandwalla and Sturtevant<sup>31</sup> demonstrated by computation that shock waves are capable of causing cell rupture by inducing unsteady flows in the surrounding media. Subsequent experimental studies<sup>65</sup> using OP to eliminate cavitation and a parabolic reflector to refocus the wave field within the sample vial showed that even in the absence of cavitation shock waves could deform foils and that cell lysis was significantly enhanced by shock wave focusing. This supports the idea that cell lysis can be caused by gradients in shock strength and validates shear as a damage mechanism.

How shear might contribute to renal injury is not known. The PReI reflector data with pigs<sup>63</sup> suggest that the magnitude of damage caused by cavitation far outweighs the injury caused by shear. However, the contribution of shear may not be entirely inconsequential. It is possible that damage caused by shear might potentiate damage caused by cavitation: i.e. it seems feasible that vessel rupture due to shock gradients could initiate bleeding into the kidney interstitium and that this pooling of blood could then support cavitation.

### **Commentary: can lithotripsy be improved?**

We see at least two logical paths that can lead to significant improvements in SWL:

1. reinvention of the lithotripter
2. rediscovery of how to use it.

Our look at the evolution of lithotripsy shows that patient outcomes were never better than during the era of the first-generation lithotripter, the unmodified Dornier HM3. Subsequent technological advances did not produce a better instrument and did not yield better results. Instead, lithotriptors have progressively become too powerful. With the widespread adoption of these machines, stone-free rates have dropped, retreatment rates are up, and reports of adverse effects are on the rise.

Recent research has made considerable progress in the effort to determine how shock waves break stones and, likewise, has improved understanding of the factors that lead to collateral tissue damage. The story is not complete, but we now know that multiple mechanisms contribute to stone breakage. Both the compressive and tensile components of the lithotripter pulse are needed to bring stones to complete comminution. The compressive phase of the shock wave does not work alone—cavitation plays an important role in stone fragmentation. Cavitation may actually be essential in breaking stones to completion.<sup>35</sup> But, cavitation is also problematic. Cavitation bubble activity (shock wave-bubble interactions) appears to be a significant, if not the dominant mechanism responsible for tissue damage.

There is an important lesson to be learned from the history of lithotripsy. We cannot expect to solve the problems associated with shock wave therapy solely from what we have learned about the physics of lithotriptors. We need to pay attention to the clinical

findings as well. When manufacturers saw that their second-generation machines did not perform to expectations, they found a solution based on laboratory results. Boosting the power of the lithotripter broke stones better *in vitro*. For example, the Storz Modulith breaks stationary artificial stones better than the Dornier HM3 lithotripter.<sup>68</sup> This result does not take into account that in a living, breathing patient it is more difficult to keep the third-generation machine on target, and that excessively powerful shock waves lead to increased trauma to the kidney.<sup>11-21</sup>

There is recent evidence for a move back to the basics. As mentioned above, a new lithotripter has been introduced that, like the first-generation Dornier HM3 lithotripter, produces low-to-moderate acoustic pressures focused to a relatively broad focal zone. Initial clinical findings with the Xi Xin-Eisenmenger machine are encouraging.<sup>23</sup> This lithotripter may not prove to be a solution to the problems that currently face SWL—independent assessment of the device is needed—but it appears to be a step in the right direction. To be sure, this machine is a departure from the trend in SWL toward high acoustic pressure devices. If this machine continues to deliver good results, it may set a new trend. We may see the development of other low-to-moderate power devices—a return to or a reinvention of the first-generation lithotripter.

On the other hand, how lithotripsy is performed may be more important than which lithotripter is used. Our endorsement of the Dornier HM3 lithotripter is a matter of siding with the lesser of two evils. We are well aware that adverse effects occur with the Dornier HM3 lithotripter. It is safe to say that any lithotripter can be used to overtreat a patient. Likewise, it seems reasonable to suggest that with the proper treatment protocol most any lithotripter can be used more effectively and with improved safety.

We would argue that there are several basic conditions of shock wave treatment that will give better outcomes. Our recommendation is to

1. use lower power
2. treat at slow shock wave rate
3. sedate the patient
4. keep the dose (number of shock waves) low.

As for power, there are no good published studies to show the effect of power setting on stone comminution. In our experience using the Dornier HM3 lithotripter (at the Methodist Hospital), we have found that most classes of stones respond well to treatment at 12–15 kV. Use of low power has been recognized to be effective in the treatment of pediatric patients. Also, initial results with the Xi Xin-Eisenmenger lithotripter report using this machine at very low power. We recommend starting treatment at low power and increasing the power only if the stone does not break up.

As for shock wave rate, there are several reports to show that slowing the rate of shock wave administration improves the effectiveness of treatment.<sup>53,54</sup> This concept was first tested *in vitro* and then demonstrated using model stones implanted in pig kidneys.<sup>53</sup> Preliminary results from the first prospective randomized clinical trial of shock wave rate show that treatment at 1 SW/s is more effective than treatment at 2 SW/s.<sup>54</sup> Also, the initial report of favorable results with the Xi Xin-Eisenmenger lithotripter describes treatment at a very slow rate (0.3 Hz, 20 SW/min).

The issue of sedation is controversial. Many patients would rather not be sedated. Many urologists would rather not sedate their patients. Many lithotriptors are intended to

be used as anesthesia-free machines. Still, there is very good evidence to show that outcomes are much better when the patient is under sedation.<sup>9</sup> This may be simply a matter of targeting the lithotripter: when the patient moves around, it is more difficult to hit the stone.

The severity of collateral damage to the kidney increases with the dose of shock waves. The fewer the number of shock waves delivered, the better. Some urologists take the position that it is better to overtreat than to retreat. We contend that it is best to monitor treatment closely and to stop as early as possible.

There may be other factors or features of treatment that can and should be improved in SWL. Shock wave coupling is one. In 'dry table' lithotripsy, transmission of shock wave energy into the body is dependent on the gel interface between the shock head and the skin. This interface can be a site for attenuation of the shock wave and possibly scattering or refocusing of the pulse. We know of no systematic study that has assessed the quality of coupling on stone comminution or on tissue injury. Imaging is also a concern. There is a good chance that in many cases the number of shock waves used in treatment is dependent on how well the urologist can see the fragments on screen. Overtreatment probably occurs more often than not because the urologist cannot see the stone well enough to know when to stop treatment. Ongoing refinements in diagnostic ultrasound and radiologic imaging should lead to advancements that will improve this aspect of SWL.

In some respects lithotripsy has been an ongoing experiment. A lot of observations have been made but few improvements have been realized. We think there is reason to expect that lithotripsy is about to change for the better. For one, awareness that SWL can cause adverse effects has never been higher. As a result, urologists are more keenly aware of the potential for collateral damage and are more likely to treat conservatively. We now know that some lithotriptors are more dangerous than others. We expect that urologists will begin to demand better instruments and that this will lead to the development of safer, more effective lithotriptors. We are beginning to learn that how shock waves are delivered—how the urologist controls the parameters of shock wave delivery—can have a significant effect on the outcome of treatment. This is a positive development and will improve how SWL is performed, regardless of the lithotripter that is used.

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## Percutaneous treatment of renal and ureteral calculi

Benjamin R Lee and Arthur D Smith

In 1955 Goodwin et al reported the use of percutaneous nephrostomy drainage for the treatment of urinary obstruction and infection.<sup>1</sup> However, the first description of extraction of renal stones through a percutaneous tract was not reported until 20 years later, when Fernstrom and Johansson used the technique successfully in 3 patients.<sup>2</sup> In 1979, Smith and colleagues reported a series of patients treated for renal and ureteral calculi via a percutaneous nephrostomy tract.<sup>3</sup> In 1984, the introduction of extracorporeal shock wave lithotripsy (ESWL) to clinical urology revolutionized the treatment of urinary calculi in a completely noninvasive approach.<sup>4</sup> Improvements in lithotripsy equipment, fluoroscopic imaging, and endoscopic instruments have continued to develop and refine the percutaneous approach to renal and ureteral calculi. This chapter will review the indications, contraindications, technique of obtaining access, patient hospital course, complications, and results.

### **Diagnosis, work-up, and staging of the disease process, including X-rays**

Minimally invasive surgery has replaced open stone surgery in the treatment of renal calculi. With the armamentarium of ESWL, ureteroscopy, or percutaneous nephrolithotomy (PCNL), the endourologist today can treat any size of calculus in a minimally invasive fashion to achieve stone-free rates between 75 and 100%.<sup>4</sup> A systematic approach is required for diagnosis and management of renal and ureteral stones. Treatment must be carefully planned to maximize the stone-free rate, factoring in calculus size, composition, location, type of surgical approach, experience of the operating surgeon, and underlying anatomy of the kidney.

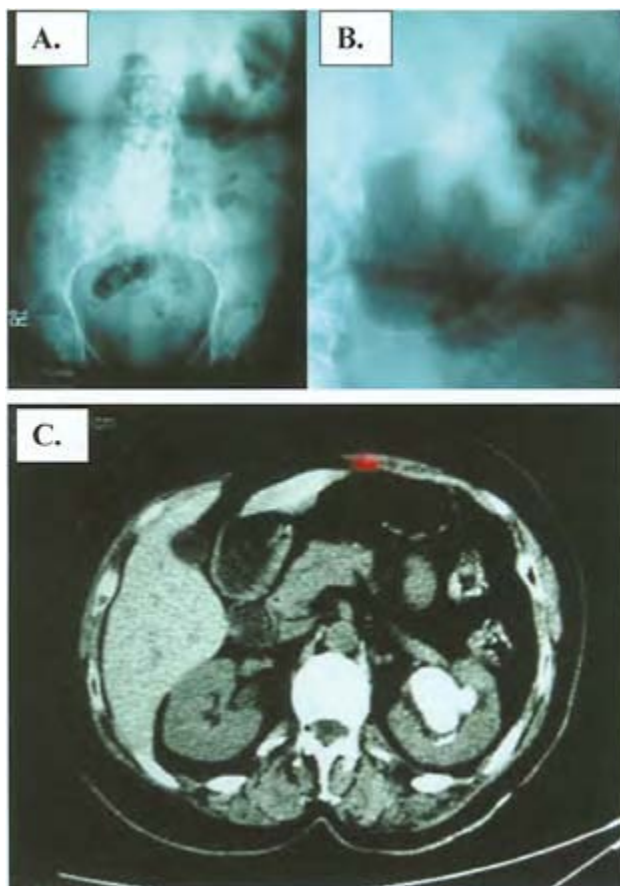
Noncontrast spiral abdominal computed tomography (CT) scanning has become the primary imaging modality to diagnose renal and ureteral calculi in the acute setting (Figure 29.1).<sup>5</sup> The helical CT scan has 95–100% sensitivity and a 96–100% specificity for diagnosing urinary calculi.<sup>6–8</sup> When delineation of the ureter and collecting system anatomy and function are required for presurgical planning or when accurate dimensions of renal calculi size are necessary, CT should be supplemented with a plain X-ray of the kidneys, ureter, and bladder (KUB) and intravenous pyelography (IVP).

### **Treatment options (operative drawings, and photographs)**

Treatment of renal and ureteral stones is based primarily on location, size, composition, and patient's anatomy. For asymptomatic calculi <1 cm in patients with sterile urine,

conservative therapy with aggressive hydration and analgesia comprise the initial management. Patients who fail conservative treatment, have a urinary tract infection, or continue to be symptomatic, progress to therapeutic intervention.

For calculi in the distal third of the ureter, rigid ureteroscopy provides superior optics, excellent image transmission, and allows direct access without a ureteral sheath. Stone-free rates of 97–100% have been achieved.<sup>9,10</sup> ESWL for distal ureteral stones <1.5 cm is an alternative; in studies using an HM3 lithotripter, success rates of 90–95% have been achieved. However, retreatment rates were higher for shock wave lithotripsy (15%) than ureteroscopy (0%) in reported series.<sup>10,11</sup> In addition, as an outpatient procedure, ureteroscopy is a more cost-effective procedure, with a lower operating cost than ESWL.<sup>10</sup>



**Figure 29.1** (A) KUB plain film of staghorn calculus. (B) Magnified view of staghorn calculus. (C) Abdominal noncontrast spiral CT image.

For calculi in the proximal third of the ureter, success rates of flexible ureteroscopy for stones >1 cm have been reported as 93%, compared with 50% for ESWL.<sup>12</sup> For stones in the proximal ureter <1 cm, success rates were 100% for flexible ureteroscopy+holmium : YAG laser lithotripsy and 80% for ESWL. Flexible ureteroscopy has improved significantly with incorporation of nitinol fibers, fiberoptic light transmission and larger working channels. Sizes as small as 7.4F allow instrument passage to the proximal ureter to fragment ureteral calculi using the holmium laser at settings of 1.0 J and a rate of 10 Hz.

Renal calculi >2.0 cm have higher stone-free rates with the percutaneous approach. Success rates have consistently been >90% with PCNL. Several investigators have also shown that the position of the stone has a significant effect on the stone-free outcome of ESWL and PCNL. The success rate for ESWL for lower pole calculi has been reported at 37% compared with the success rate of 95% in a multi-institutional study comparing symptomatic lower pole calculi.<sup>13,14</sup> Based on these results, PCNL is often considered the treatment of choice for lower pole renal calculi >1 cm.

### Indications and contraindications of procedures discussed

Indications for the percutaneous approach to the kidney include patients with associated anatomic abnormalities, such as ureteropelvic junction (UPJ) obstruction, infundibular stenosis, or calyceal diverticulum. The percutaneous approach, as opposed to ureteroscopic or shock wave lithotripsy, is reserved for stone burdens, including staghorn calculi, renal pelvic stones >2 cm, and lower pole stones >1 cm. Patient characteristics, including obesity, scoliosis, renal artery or aortic aneurysms, or patient preference are also key factors. Finally, indications for PCNL include treatment failures of other modalities such as ESWL, or previous attempted ureteroscopy for lower pole stones or calyceal calculi (Table 29.1). Stones composed of cystine or calcium oxalate monohydrate are at increased risk of SWL failure, due to the hardness of stone composition.

Currently, the only absolute contraindications to percutaneous stone extraction are irreversible coagulopathy and active, untreated urinary tract infection.

**Table 29.1** *Indications for percutaneous nephrolithotomy*

1. Stone burden:
  - a. Staghorn calculi
  - b. Renal pelvic stones >2 cm
  - c. Lower pole stones >1 cm
  - d. Stones associated with upper tract foreign bodies
2. Anatomic abnormalities:
  - a. UPJ obstruction
  - b. Associated distal ureteral obstruction
  - c. Infundibular stenosis
  - d. Calyceal diverticulum
3. Patient characteristics:

- a. Obesity
  - b. Scoliosis
  - c. Renal artery or aortic aneurysms
  - d. Patient preference
4. Treatment failures:
- a. Failure of ESWL
  - b. Previous attempted ureteroscopy
5. Stone composition:
- a. Cysteine
  - b. Calcium oxalate monohydrate
- ESWL, extracorporeal shock wave lithotripsy; UPJ, ureteropelvic junction.

### Patient and preoperative preparation

All patients should be advised of the therapeutic options of percutaneous stone extraction, ureteroscopy, or ESWL. The vast majority of patients will ultimately benefit from a single procedure to render them stone free. Preoperative planning includes either IVP or a noncontrast abdominal CT scan. Informed consent, including risk of bleeding requiring transfusion, infection, injury to adjacent organs, possibility of hydrothorax, or pneumothorax, should be discussed. In complex cases, the potential for a return procedure to the operating room for a second look should be discussed with the patients.

Standard preoperative preparation includes typing and crossing the patient's blood. Patients undergoing initial PCNL undergo general endotracheal anesthesia. If a patient needs a second-look procedure, local anesthesia can suffice. A first-generation cephalosporin or broadspectrum antibiotic based on urine culture sensitivity is administered intravenously prior to initiation of the procedure.

### Recommended equipment or instruments

Recommended equipment for percutaneous nephrolithotomy is shown in Figure 29.2, with a list of instruments given in Table 29.2.



**Figure 29.2** Percutaneous nephrolithotomy table setup. Standard procedure setup includes nephroscope, Amplatz dilator set, 18 gauge access

needle, J tip and stiff guide wire,  
nephroscope graspers, and ultrasonic  
lithotripter.

**Table 29.2** *Instrument list*

- a. Nephroscope, 0° lens with 26F sheath
- b. Amplatz dilator set (8F-30F dilators 4- sheaths) vs balloon dilation set
- c. 0.038 inch J tip guide wire
- d. 0.038 inch stiff torque wire
- e. 18-gauge access needle
- f. 6F open-ended ureteral catheter
- g. Fluoroscopic X-ray
- h. Ultrasonic lithotripter
- i. Nephroscope graspers, biopsy forceps
- j. Hypaque (diatrizoate meglumine+diatrizoate sodium), diluted 30%

### **Approach and helpful tips**

The technique for creating access tracts is now discussed.

Prior to gaining percutaneous access, the patient must have a 6F open-ended ureteral catheter placed to help define the anatomy, as well as allow subsequent retrograde pyelography and distention of the collecting system if needed. Placement of this ureteral catheter will also provide the ability to achieve antegrade ureteral catheterization following retrieval from above, as well as achieve through and through access. Complete evaluation of the renal collecting system is imperative prior to definitive percutaneous puncture for access tract creation.

Typically, fluoroscopic guidance is used, with either retrograde or antegrade visualization of the collecting system or direct percutaneous access to a visible stone. If cystoscopic retrograde ureteral access is first achieved, injection of contrast material can help opacify the collecting system. Initial injection of air can also help define the collecting system prior to needle placement, as well as help differentiate anterior from posterior calyces. Following initial needle placement, retrograde injection of air should be avoided due to the risk of an air embolus. Retrograde contrast injection following an initial attempt should also be avoided because extravasation of contrast could obscure the calculus. Alternatively, visualization of the collecting system can be achieved via intravenous contrast injection just prior to start of the procedure, or by direct percutaneous puncture with a 22-gauge Chiba needle, placed one or two fingerbreadths lateral to the first or second lumbar transverse process. After initial passage, gentle aspiration is performed until urine appears, at which time radiographic contrast material is directly injected to opacify the collecting system. Once the collecting system is visualized, percutaneous access to the desired calyx is established.

Following ureteral catheter placement in the dorsal lithotomy position, the patient is repositioned prone on a fluoroscopic table, with appropriate padding to elbows, wrists, chest, knees, and ankles (Figure 29.3). Alternatively, the procedure may begin from the

prone position on a split-leg fluoroscopic table, with placement of the ureteral catheter performed using a flexible cystoscope. The prone position allows access to the posterolateral flank. Following Betadine (povidone-iodine) skin prep, alcohol is applied in order to enhance adhesion of the surgical drapes. Currently, we use a full-length endourology drape that has a plastic side pouch for collection of irrigant fluid. Suction drainage tubing can be applied to the side pouch for optimal drainage. A sterile drape is attached to the C-arm to allow surgeon manipulation. The C-arm must have a rotation ability of more than 90° as well as a memory function to save a previous image on an adjacent screen. The source of radiation emission from the C-arm is positioned beneath the patient to minimize exposure to the surgeon and nursing staff. Lead aprons and thyroid shields should be mandatory equipment worn by all operating room personnel, as well as radiation monitor badges.

The ideal percutaneous access tract is located in the posterior axillary line, via the posterior calyx, because major vessels surrounding the pelvis are avoided. The ideal tract courses through the posterior lateral flank, through the renal parenchyma, into the tip of a posterolateral calyx, and in a direct line with the middle of the renal pelvis. The transparenchymal portion of the tract stabilizes the nephrostomy tube and provides a seal around the tube, preventing urine extravasation into the perinephric space. A target mid pole calyx or upper pole calyx is optimal over a lower pole initial access in order to allow subsequent instrument maneuverability without tearing renal parenchyma.

The skin insertion site may be placed more laterally in obese patients in whom the lateral segment of the colon is displaced ventrally. In patients with abnormal abdominal

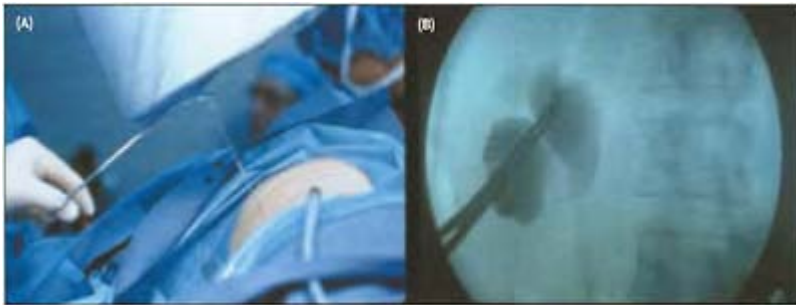


**Figure 29.3** Patient positioning. Great care is taken to pad all joints. Additionally, bolsters can be used under the chest to elevate the upper torso.

anatomy, such as following jejunal-ileal bypass or horseshoe kidneys, the position of the kidney relative to the colon may be distorted. These patients are at a higher risk for a transcolonic needle placement. For horseshoe kidneys, the access tract is virtually perpendicular to the plane of the back, in a paraspinous, medial position. One must also

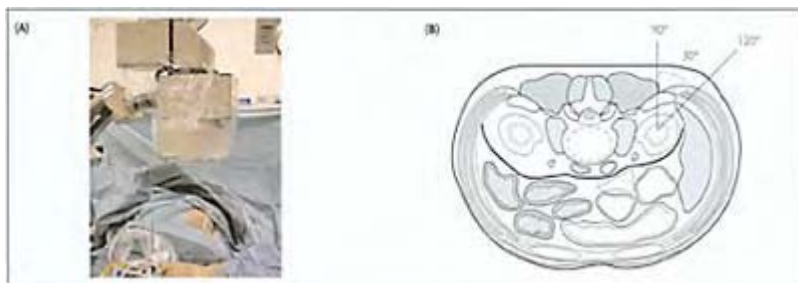
take into consideration that a more medial insertion site is uncomfortable for the patient, who invariably lies supine after the procedure, and can lead to compression and kinking of the external portion of the nephrostomy tube into the back. A subcostal approach lowers the risk of pneumothorax. Puncture of anterior calyces is required only if access to the posterior calyces is not possible. Access from an anterior calyx to the renal pelvis is very difficult because of the inherent difficulty in directing a wire backwards. Direct puncture of the renal pelvis should also be avoided, due to the significant risk of injury to the posterior branch of the renal artery.

C-arm fluoroscopy is used to help localize the target calyx, using a triangulation method of two different views. A Seldinger technique-based access is commenced with the C-arm positioned at 120° angle, and a target calyx is identified. The ideal site provides the shortest tract to the calyx from below the 12th rib. Visualization with the C-arm at 90° defines the medial, vertical plane for entry to the calyx. The C-arm is then rotated 30° towards the surgeon (Figure 29.4). This places the angle of the C-arm (total of 120°) in the same central posterior plane of the kidney, as well as providing a direct end-on view of the posterior calyces. With the C-arm at 30°, the skin site over the target calyx is marked. A vertical line, inferiorly, is drawn to a point of 1–2 cm below the 12th rib. This site is marked and serves as the site of needle entry. An 18-gauge needle is inserted at this point to the level of the target calyx, and then the C-arm is rotated back to 90° to finalize the depth of penetration (Figure 29.5).



**Figure 29.4** C-arm at 30° towards the surgeon. (A) A metal cryl can be used to help position the needle over the target calyx. (B) Fluoroscopic view of needle creates a 'bullseye' over the dilated collecting system as the needle is inserted.





**Figure 29.5** (A and B) C-arm, 90° to finalize triangulation of needle insertion. After initial insertion of the needle in the 30° view, the final depth of penetration is performed under the 90° view.

A hemostat can be used to hold the needle and minimize radiation exposure to the surgeon's hand. To confirm entry into the collecting system, the inner obturator is removed from the needle, and one should see efflux of urine. Alternatively, one can aspirate urine to confirm entry. Small amounts of diluted contrast may be injected to confirm the intracalyceal position of the needle tip if fluoroscopic guidance is used, but it may result in extravasation and obscure the collecting system. A soft-tipped 0.038 inch floppy-tip J guide wire is then inserted through the needle and directed to coil in the calyx, advance across the calyceal infundibulum, and into the renal pelvis for stability.

Guide wire stabilization and wire advancement into the renal pelvis or across the UPJ is crucial for subsequent tract dilation to prevent accidental wire dislodgement. If that position cannot be achieved, a sufficient amount of wire should be coiled in the renal pelvis to prevent guide wire dislodgement. One can bend an 8 or 1 OF catheter to help direct advancement and position of wire passage (Figure 29.6).

Once access to the collecting system is achieved, a 1 cm skin incision is made at the wire site. Tract dilation can proceed using Amplatz serial dilators, metal coaxial dilators, or high-pressure balloon dilation. These are all designed to be inserted over a working wire: either 0.035 inch or 0.038 inch wires are most commonly used. Amplatz dilators should be used over an 8F catheter, which in turn is placed over the wire. This will add increased rigidity and prevent kinking and buckling of the wire with subsequent dilations.

Serial dilations to 30F are then performed, with final placement of the 34F sheath over a dilator.

The individual Amplatz dilators are also relatively rigid and, in combination with the stiffer working wire-catheter



**Figure 29.6** Use of 10F catheter to help direct placement of the guide wire.

complex, allow acute tract dilation through rigid scar tissue in nearly all patients. All dilation passages should be performed under fluoroscopic guidance in order to monitor depth of insertion. The tip of the dilator should not be advanced across the UPJ upon initial dilation to decrease the possibility of collecting system tears or ureteral avulsion. Although there is a theoretical risk of increased renal parenchymal bleeding generated by shearing forces of the angled catheter tips, this has not been shown to be a clinically significant concern. If a guide wire develops an acute angular kink during tract dilation, immediate replacement is warranted to prevent subsequent catheter manipulation problems.

Balloon dilation is performed by advancing the device over a wire, and positioning the radiopaque marker proximal to the infundibulum. Dilation of the tract is performed using a high-pressure syringe at pressures up to 15 atm. Balloon lengths of 15 cm and 30F can be used. With a single balloon inflation, the entire access tract is dilated in a short time. Fluoroscopic monitoring of the balloon dilation is performed until the waist that appears at the renal capsule disappears. Although these balloons are easy to use, they are more expensive than alternative dilating methods and, after initial use, may not pass easily over a wire for subsequent dilations.

It is important to have all instrumentation—nephroscope, camera, lithotripter device (ultrasonic, holmium laser, electrohydraulic lithotripter (EHL))—set up prior to final dilation of the access tract. Immediate placement of the rigid nephroscope through the 34F sheath using normal saline irrigation helps to improve visualization and remove possible blood clots. At most institutions, normal saline is the irrigant of choice, since it prevents hyponatremia that may result from intravascular absorption when hypotonic solutions are used. Care is taken to avoid



**Figure 29.7** Amplatz dilator. Serial dilation over an 8F catheter/guide wire system allows serial dilation up to 30F.



**Figure 29.8** Ultrasonic lithotripter. The benefit of the ultrasonic lithotripter is fragmentation of the calculus combined with continuous suction of small fragments.

inadvertent over-advancement of instruments or the access sheath, as this will likely cause a laceration of a renal infundibulum or renal pelvis.

Once visualization of the calculus has been achieved, systematic fragmentation and removal of renal calculi is commenced using either EHL, holmium laser, or ultrasonic lithotripter. We prefer the ultrasonic lithotripter, as fragmentation is combined with active suction removal of calculi fragments. Ultrasonic lithotripsy is based on the principle of the piezoelectric effect demonstrated by Curie in 1880. When a piezoceramic crystal has an electric charge applied to it, vibrations result at a specific frequency (23,000–27,000 Hz).<sup>15</sup> The vibrations of the crystal produce ultrasonic waves, which can be transmitted down the shaft of a metal hollow probe, resulting in a lithotripsy effect at

the tip of the metal probe. Therefore, for the ultrasonic lithotripter to be effective, it must be in direct contact with the stone (Figure 29.8). Fragments less than 9 mm or 10 mm in diameter may be small enough to be withdrawn intact through the access sheath. These stones are grasped under direct visualization with the rigid graspers or endoscopic forceps.

One alternative method of stone extraction in situations of calyceal calculi lying at acute angles to the percutaneous tract is to use flexible nephroscopy in combination with a nitinol stone retrieval basket. Although flexible nephroscopy may occasionally be successful during the initial percutaneous procedure, even a small amount of bleeding can obscure the visual field. Therefore, flexible nephroscopy is generally reserved for second-look procedures and is generally more successful through a mature tract.

Percutaneous management of ureteral calculi can be addressed if concomitant ureteral stones exist within the renal pelvis or collecting system calculi as a secondary approach. Proximal ureteral calculi are optimally treated with either flexible ureteroscopy or ESWL. Patients with urinary diversion in whom retrograde identification of the ureteral orifice may prove difficult are candidates for the percutaneous approach. For stones at the UPJ, direction of the rigid nephroscope to that level allows retrieval using the rigid graspers under direct visualization. For stones in the ureter, a flexible cystoscope or ureteroscope allows lithotripsy using the holmium laser and retrieval of residual fragments using a nitinol basket (Figure 29.9). To aid in positioning of the instrument in the ureter, passage over a floppy-tip guide wire can be used. After the stone is treated, assessment of the integrity of the ureter at the location of the calculus must be made with an antegrade pyelogram. Perforations should be identified and small areas of extravasation treated with an indwelling ureteral stent.

Once identification of the previously placed ureteral catheter is achieved, a stiff guide wire can be passed to achieve through and through access (Figure 29.10). Access in this manner ensures a maximum spectrum of options for urinary drainage at the completion of the procedure. Once all the stone has been fragmented and cleared by endoscopic and radiographic visualization, the choice of



**Figure 29.9** Nitinol stone retrieval basket.



**Figure 29.10** Ureteral catheter. Once identification of the ureteral catheter is achieved, through and through access can be achieved and allows optimal urinary drainage at the end of the procedure.



**Figure 29.11** Urinary re-access sheath. Proximally, this catheter is 24F with a Malecot portion to hold the catheter within the renal pelvis. Distally, the ureteral portion tapers down to 8F.

an appropriate nephrostomy tube to be inserted through an acute tract depends on the desired function of the catheter. Our preference is a combined Malecot nephrostomy catheter with attached ureteral catheter. Proximally, the intrarenal portion of the re-entry catheter is 24F, with the distal ureteral portion tapering down to 8F (Figure 29.11). This catheter allows external drainage with the Malecot tip in the renal pelvis, while its distal tip lies across the UPJ, maintaining access to the ureter. This allows easy access for subsequent nephrostograms to determine further therapy or removal of both ureteral and renal drainage catheters in one step. If prolonged ureteral drainage is desired, an internal double J ureteral stent can be placed in combination with a council-tip catheter to the kidney. If council-tip catheters are not available, a hole at the distal end of a Foley catheter can be created using a catheter punch or slit created using a No. 11 blade. A

Foley catheter is placed and nephrostomy tube secured to the skin to prevent inadvertent dislodgement. A nephrostogram is performed at the end of the procedure to ensure adequate drainage down the ureter and optimal positioning of the nephrostomy tube.

### **Common and unusual intraoperative, acute, and longterm postoperative problems and how to identify them**

Complications associated with PCNL are usually minor and include hemorrhage, pneumothorax, hydrothorax, perforation of the collecting system, and injury to adjacent organs. Significant bleeding from the nephrostomy tract may be treated with temporary tamponade of the drainage catheter. In the setting of hypotension, anemia, and unstable vital signs, transfusion and subsequent angiography with potential embolization of identified vessels may be performed (Figure 29.12).



**Figure 29.12** Arteriogram demonstrating (A) source of hemorrhage and (B) following embolization with coils.

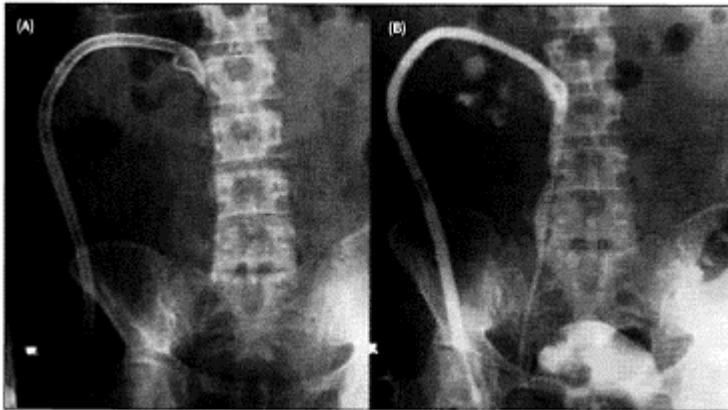
### **Results such as success rate, length of hospital stay, and complication rates**

Patients are advanced to a regular diet immediately after recovery from anesthesia. Furthermore, they undergo an antegrade nephrostogram on postoperative day 2 (Figure 29.13). If the study demonstrates immediate drainage down the ureter, with no extravasation, the re-entry renal-ureteral catheter is removed prior to patient discharge. If extravasation of urine is demonstrated on an antegrade nephrostogram, the nephrostomy

tube is left for external drainage for an additional day or until resolution of the extravasation occurs. Upon removal of the re-entry catheter, the majority of patients will seal typically within 24 hours. For a minority of patients who may have persistent drainage from the skin nephrostomy site, it may be due to blood clots, which will typically lyse, or ureteral edema, which will resolve spontaneously. If there is significant, prolonged drainage at the skin site, an external collection bag may be placed to monitor output. It is the rare patient who requires placement of an internal ureteral stent to decrease external leakage through the skin site, and generally the stent is reserved for patients with more than 1 liter of urine drainage from the skin site.

### **Conclusion and future unique and innovative treatment options currently undergoing testing**

In conclusion, PCNL is the established standard of care for treatment of complex renal calculi. Stone-free rates are consistently greater than 90% and approach 100% at tertiary care centers.<sup>16–18</sup> Morbidity of PCNL is acceptably low, with preservation of renal function.<sup>19</sup> Future directions in percutaneous stone treatment include the continued development of instrumentation, with combination of pneumatic and ultrasonic lithotrites into one instrument.<sup>20</sup> This technology appears promising for expeditious removal of renal calculi. Furthermore, robotic percutaneous needle placement has been incorporated into a system to allow remote needle placement under radiologic guidance.<sup>21</sup> Robotic technology may play a role in future remote access placement.



**Figure 29.13** Postoperative nephrostogram. (A and B) KUB and antegrade nephrostogram demonstrating no extravasation with immediate drainage of contrast to the bladder.

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## Retrograde endoscopic treatment of renal stones: indications and technique of retrograde intrarenal surgery

Gerhard J Fuchs and J Paul Yurkanin

### Introduction

Interventional management of kidney stones has changed dramatically over the last two decades with the development of extracorporeal shock wave lithotripsy (ESWL) and endourologic procedures, such as percutaneous renal surgery (PRS) and retrograde intrarenal ureterorenoscopic surgery (RIRS). Technical refinements coupled with prudent application of the new treatment modalities of minimally invasive surgery have greatly improved patient care, resulting in high stone-free rates with reduced morbidity and shortened recovery. Open surgical techniques are practically obsolete for the vast majority of kidney stone patients, with the exception of complex reconstructive procedures.<sup>1-9</sup>

Extracorporeal shock wave lithotripsy—initially introduced in 1980 in Munich, Germany—has revolutionized the management of renal stones and is the treatment of choice for the majority of patients with uncomplicated renal stone disease.<sup>1-9</sup> In 2003, approximately 70% of patients with renal stones were treated with ESWL monotherapy, achieving acceptable stone-free rates. Additionally, 15% of patients with more complex stones can receive ESWL treatment in conjunction with endoscopic surgery. The remaining 10–15% of patients either require endoscopic surgery alone (PRS or RIRS) or open surgery (1–3%). Key to successful stone management is proper patient selection, acknowledging the limitations of the ESWL technology, and knowing the limits of one's own endourologic expertise.<sup>8-10</sup> In this chapter we review the differential indications of renal stone treatment, with special consideration of the role and surgical techniques of RIRS.<sup>11-15</sup>

### Differential indications for renal stone treatment

The criteria for the selection of the appropriate treatment for renal stones are:

1. stone burden
2. intrarenal and upper urinary tract anatomy (including the patient's body habitus)
3. concomitant medical disease
4. patient compliance (Table 30.1).

Solitary stones or multiple stones of an added diameter of up to 2.5 cm are considered ideal conditions for ESWL treatment, provided there is no hindrance to the spontaneous elimination of gravel (anatomic or physiologic). Stone clearance rates of between 90%,

for stones of 1 cm in the renal pelvis, and 70%, for solitary/multiple stones of up to 2.5 cm, can be expected (with exception of lower pole location). Although it has been shown that even staghorn stones can be treated with ESWL monotherapy, larger stone size yields lesser stone-free rates, necessitating more frequent retreatment.<sup>8–10,16–17</sup> The need for the passage of a larger amount of gravel is fraught with higher complication rates such as ureteral obstruction, obstructive pyelonephritis, and a prolonged period of stone passage, resulting in unpredictability of outcome and the more frequent need for auxiliary procedures.<sup>10</sup> Therefore, larger stones and those associated with anatomic abnormality of the renal collecting system or upper urinary tract are better treated with endoscopic surgery.<sup>8,15,17,18</sup> Of the two endoscopic surgery approaches, the percutaneous antegrade approach (PCNL; percutaneous nephrolithotripsy and

**Table 30.1** *Differential indications for endoscopic treatment of kidney stones*

| Criteria             | ESWL   | RIRS   | RIRS-SWL                                  | PCNL   |
|----------------------|--|--|---|--|
| Stone size (primary) | <2.0 to 2.5 cm   | <1.5 to 2.0 cm                                     | >1.5 to 2.5 cm                            | >2.5 cm  |
| Composition          | Calcium oxalate dihydrate; calcium oxalate monohydrate; struvite | Need to be stone free; all compositions            | Occasionally staghorn; all compositions   | Need to be stone free; all compositions                              |
| Anatomy              | Normal   | Abnormal; urinary diversion                        | Normal; urinary diversion                 | Abnormal; urinary diversion  |
| Physiology           | Normal   | Abnormal; size <1.5 cm                             | Normal                                    | Abnormal; size >1.5 cm   |
| Residual stones      | 5 mm and less; no stent; anesthesia-free                         | All sizes <1.5 cm; <50 fragments; abnormal anatomy | 1.5–2.5 cm; <50 fragments; normal anatomy | All sizes >2.5 cm; any number of fragments; grossly abnormal anatomy |

ESWL=extracorporeal shock wave lithotripsy; RIRS=retrograde intrarenal surgery; RIRS-SWL=concomitant use of RIRS and SWL in the same treatment session; PCNL=percutaneous nephrolithotripsy and stone removal.

stone removal) is usually chosen for the more complex stone conditions (Table 30.1), whereas the lesser invasive approach of RIRS is the choice for patients with moderately complex stone conditions (Table 30.2).

### Indications for RIRS

We now describe the common indications for RIRS as well as give a detailed account of the authors' choices for RIRS and the technical aspects of this approach.

Historically, RIRS was first employed in the late 1980s for the management of retained stones that had failed ESWL treatment.<sup>11–15</sup> These stones were usually found well fragmented and located in the lower calyces, from where they could be retrieved with stone baskets or graspers. A second subset of initial patients undergoing RIRS were patients with failed ESWL treatment for stones contained in calyceal diverticuli (mostly

of the upper and mid calyces).<sup>13</sup> Success with these and further refinements of the technology in terms of smaller instrument design (7.5F instead of 10.4F; 1990), new energy sources (holmium laser; 1994), and the use of stone retrieval devices better suited for the kidney (tipless basket design; 1997, access sheaths; 2000) have promoted the use of RIRS into becoming a routine procedure for an increasing number of kidney stone conditions.

As of 2003, the indications for primary RIRS at our institution are as depicted in Table 30.2. For these indications, RIRS has become the treatment of choice because it is a minimally invasive outpatient procedure with success rates superior to ESWL and low perioperative morbidity.<sup>18–23</sup> The transition to the employment of the more invasive percutaneous renal surgery approach has not been fully defined as yet, and randomized studies are needed. In short, it is the authors' practice to employ RIRS as the primary choice for all stone cases where success with ESWL is doubtful and the stone burden and complexity too low to warrant the more invasive approach of PCNL (Table 30.1). This includes single stones up to 2.0 cm of any location within the renal collecting system, especially when the composition is known as calcium oxalate monohydrate (COMH), cystine, or uric acid (radiolucent). Stones in patients with nephrocalcinosis are also best addressed with RIRS, as are select patients with concomitant ureteropelvic junction (UPJ) or intrarenal stenosis. In patients with ureteral stones and concomitant renal stones (<1.5 cm), we usually treat both entities in the same treatment session using the retrograde approach.

A combination of RIRS and simultaneous ESWL can be employed for larger stone burdens, especially when multiple intrarenal locations are involved. Anatomic alterations of the renal collecting system precluding spontaneous passage of fragmented stone material require endourologic or open surgical procedures and are another indication for RIRS.<sup>16</sup> In this scenario, ESWL should only be employed as an auxiliary procedure or better not at all. Depending on stone size, location, and complexity of the

**Table 30.2** *Indications for retrograde intrarenal surgery*

**Stone disease:**

---

|  |
|--|
| Failed ESWL (solid stones <1.5 cm, less than 50 particles)   |
| Solid primary stones (<1.5 cm; <2.5 cm for RIRS-SWL)   |
| Lower calyceal stones < 1.5 cm associated with anatomic and/or functional abnormalities of renal collecting system |
| Radiolucent stones <1.5 cm (after failed medical therapy)  |
| Concomitant ureteral and renal stones (when renal stone <1.0 cm)   |
| UPJ stenosis and stones (<1.0 cm)  |
| Stones and intrarenal stenosis   |
| Stones in calyceal diverticuli (upper pole and mid renal calyces)  |
| Stones and nephrocalcinosis  |
| Stones and solitary kidney   |
| Stones and urinary diversion (conduit)   |
| Staghorn stones (rare, when ESWL and PCNL may not be technically feasible or for RIRS-SWL)                         |
| Morbidly obese patients with renal stones  |
| Patients with renal stones and coagulopathy  |

Aviation pilots (need to be free of stones)

ESWL=extracorporeal shock wave lithotripsy; RIRS-SWL=concomitant use of retrograde intrarenal surgery and SWL in the same treatment session; PCNL=percutaneous nephrolithotripsy; UPJ=ureteropelvic junction.

anatomic alteration, either retrograde ureteroscopic intrarenal surgery or—in more complex cases—percutaneous endoscopic renal surgery is the treatment of choice and few cases of very complex anatomic alterations require open surgery. RIRS is performed with flexible ureteroscopes through the intact upper urinary tract or through the reconstructed urinary tract after cystectomy. Percutaneous renal surgery is performed (usually by the radiologist or urologist under fluoroscopic and/or ultrasound control) through a percutaneous access.

Common anatomic abnormalities suitable for the RIRS approach are either secondary to abnormal position of the kidney (patient habitus, pelvic kidney, transplant kidney, horseshoe kidney), the number of renal units (solitary kidney, duplex kidney), parenchymal abnormalities (medullary sponge kidney, nephrocalcinosis, multicystic kidney disease), outflow problems (calyceal diverticuli, UPJ stenosis, ureteral stenosis, urinary diversion and reconstructed upper urinary tract, hypomotility of renal/ureteral pacemaker), and, rarely, concomitant medical problems (coagulation disorder) (see Table 30.2).<sup>16</sup> These conditions will be discussed in detail in the following, again with special attention to the use and technical aspects of RIRS.

## **Basic techniques of retrograde intrarenal surgery**

### *Instrumentation*

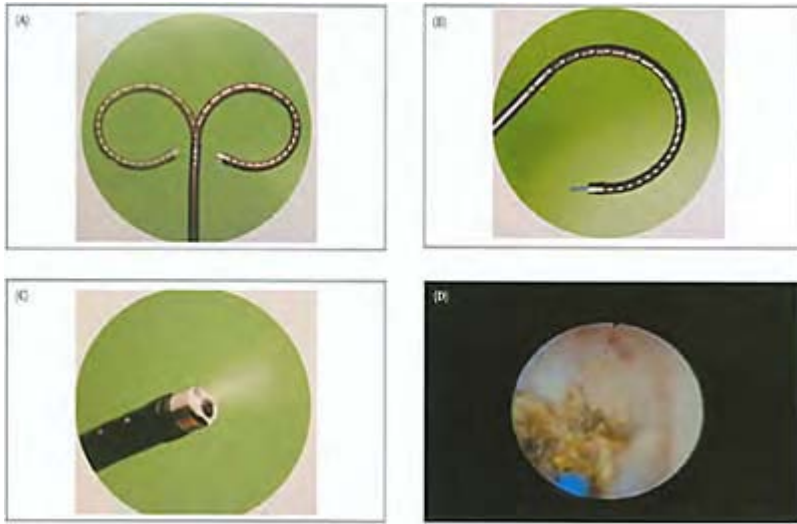
The major components of equipment for RIRS are flexible ureterorenoscopes, flexible accessories for stone fragmentation and retrieval, a suction pump, a laser lithotripsy energy source (holmium, Alexandrite, and tunable dye), a video camera system, and fluoroscopy equipment (Figure 30.1). If a laser energy source is not available, an electrohydraulic lithotripsy (EHL) device and/or the flexible probes of the pneumatic lithotrite (Swiss LithoClast, EMS-Boston Scientific Corp., Natick, Massachusetts) can be utilized.

RIRS, as the direct extension of flexible diagnostic endoscopy, has been made possible by the development of actively deflecting fiberoptics instruments and accessories appropriate for stone fragmentation and retrieval in the late 1980s.<sup>11–15</sup> Continued improvements in instrument design, especially the downsizing of the outer diameter without compromising the instrument's versatility, have facilitated access into the upper tract for the purpose of executing surgical procedures of stone treatment, stricture,



**Figure 30.1** The flexible ureteroscope (A) and the semi-rigid 9.5F (B) are used for upper tract access and RIRS.

and tumor management (Figures 30.1 and 30.2). Small-caliber, flexible endoscopes are now provided by all major manufacturers of endoscopic urologic equipment (Table 30.3). Presently, flexible ureterorenoscopes feature a small outer diameter (6.9–7.9F), working channels of 3.6F, and deflecting capabilities of up to 180° (and 120–180° in a second plane in some designs). Some of the most innovative designs being presently introduced feature 270° deflection in two planes and improved durability (FlexX, Karl Storz Endoscopy, Culver City, California) (see Figure 30.2). Accessories needed for retrograde stone manipulation and extraction include 2.0F flexible two- and three-pronged graspers and various flexible baskets (2–3F) for the removal of stone and debris. In addition, accessories for stone fragmentation include 200–300  $\mu\text{m}$  laser fibers (holmium, tunable dye, Alexandrite, or Nd:YAG lasers), 1.6F electrohydraulic probes, and 1.9F flexible pneumatic probes.<sup>19–23</sup>



**Figure 30.2** (A) New instrument design for flexible ureteroscopic with 270° upward and downward deflection. (B) New technology allows deflection of scope with 200  $\mu\text{m}$  fiber advanced to 250°. Note that the fiber is first advanced with the instrument straight until the fiber is visualized outside the work channel; only then the instrument is deflected. (C) A 7.5F tip and 8.4F shaft combine ease of access and increased durability of scope. A 3.6F work channel allows sufficient irrigation and suction when 200  $\mu\text{m}$  laser fiber or 1.9F retrieval accessories are inserted. (D) The tip of the laser probe has to be visualized at all times to avoid damage to the instrument or injury to adjacent tissue.

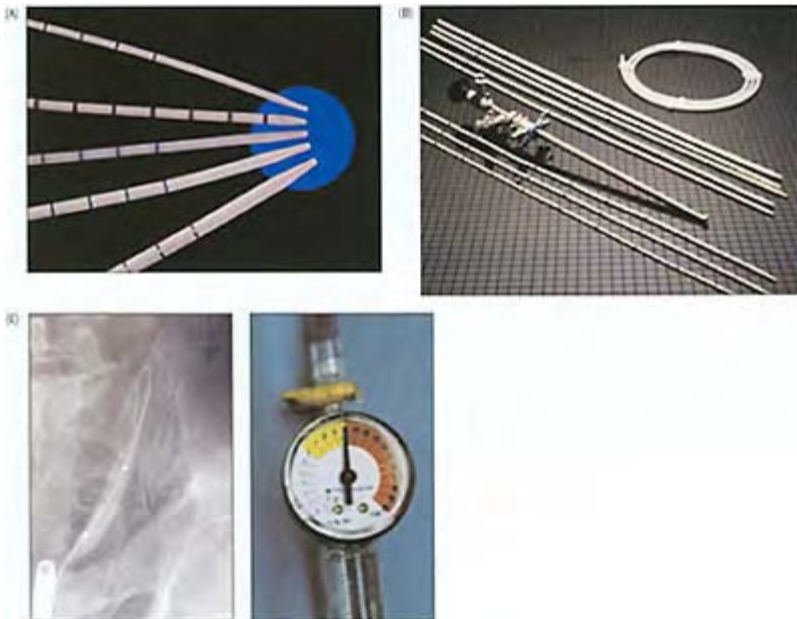
**Table 30.3** *Flexible ureteroscopes—specifications*

| Scope type | Tip diameter (F) | Body diameter (F) | Channel diameter (F) | Active deflection (downward; degrees) | Active deflection (upward; degrees) | Pixels |
|------------|------------------|-------------------|----------------------|---------------------------------------|-------------------------------------|--------|
|------------|------------------|-------------------|----------------------|---------------------------------------|-------------------------------------|--------|

|                         |     |     |     |     | degrees) |      |
|-------------------------|-----|-----|-----|-----|----------|------|
| Storz<br>(11274AA)      | 7.5 | 8.4 | 3.6 | 170 | 120      | 3500 |
| ACMI (AUR<br>7)         | 7.4 | 7.5 | 3.6 | 160 | 120      | 3400 |
| Wolf<br>(7325.171)      | 7.5 | 7.5 | 3.6 | 160 | 130      | 5000 |
| Mitsubishi<br>(971 101) | 7.9 | 7.9 | 3.6 | 134 | 170      | 6000 |
| Olympus<br>(URF-P3)     | 6.9 | 8.4 | 3.6 | 180 | 180      | 5500 |

Ureteral dilators and access sheaths are optional accessories and their role is discussed later in the section on access (Figure 30.3).

The short durability of the small flexible ureterorenoscopes, along with high purchasing and maintenance costs, has been an issue that has hampered the wider distribution of RIRS. Cautious handling and deployment of accessories—especially energy sources—as well as good and cautious handling during cleaning and sterilization can greatly prolong the lifespan of these delicate scopes. A recent survey of several manufacturers revealed that 60% of instrument damage is due to inappropriate handling of laser fibers.<sup>24</sup> Several points need emphasizing here. First, the tip of the laser fiber (especially the 200  $\mu\text{m}$  fiber) is very sharp and should only be advanced with the distal segment of the scope being straightened out. When the scope needs



**Figure 30.3** (A) Serial Teflon ureteral dilators (6–12F; optional to 16F) (B) Six to 8F ureteral dilators are passed through the work channel of the cystoscope over a working wire; larger dilators are passed over the working wire under fluoroscopic control. (C) Optional balloon dilation with 6F balloon dilator (dilation to 14F, pressure 10 Atm).

to be deflected to reach the stone, the fiber is advanced until it can be seen in the field. The fiber is then pulled back to the edge of the work channel, while the turn into the calyx is performed. The instrument is then advanced until the stone is in central vision (see Figure 30.2B). At this point the fiber is approximated to the stone (see Figure 30.2D). For safe use (patient and instrument) the laser fiber and action has to be visualized at all times. One needs to be aware that the tip of the fiber decays with use, especially when higher energy settings are chosen. Accordingly, the fiber has to be readvanced to prevent burn damage of the tip of the scope. Even a short burst of laser activation with the fiber still in the work channel may destroy the lens, the deflection cable, or the deflection rings, necessitating costly repair or replacement of the instrument. Along these lines, reusable laser fibers need to be carefully checked and tested for bends and cracks and the condition of the distal tip before being re-employed, for any damage to the laser will cause the fiber to ‘leak’ energy and eventually destroy the work channel and the scope. Before the advent of laser technology, the most common cause of instrument failure was during the cleaning and sterilization process. Naturally, the personnel in charge of cleaning and sterilization need to handle these delicate instruments with care and follow manufacturers’ instructions for safety and handling. With strict adherence to the manufacturers’ manuals, durability problems can be greatly reduced, which again puts the onus on the urologist, as team leader, to assure compliance.

### *Patient preparation*

It is of the utmost importance that patients considered for RIRS have sterile urine at the time of the procedure.<sup>13,15,18</sup> The urine is usually checked 10 days prior to the procedure and, if positive, oral antibiotics are started 8 days prior to the treatment, according to sensitivity testing. The urine is then retested 3 days prior to RIRS to ensure eradication of the infection. Routine imaging studies include plain X-rays (KUB; kidney, ureter, and bladder) and intravenous pyelography (IVP) studies or computed tomography (CT) urogram studies, which are now more commonly used. The imaging studies provide the necessary information to assess the stone burden and the intrarenal and ureteral architecture. A KUB radiography is always obtained (ultrasound if the stone(s) is radiolucent) before induction of anesthesia to reassess the stone condition and confirm the appropriateness of the treatment plan. For complex stone conditions patients are



usually also consented for percutaneous renal surgery so that intraoperative conversion to PCNL can be performed under the same anesthesia at the surgeon's discretion.

### *Anesthesia*

RIRS can be performed under any kind of anesthesia, from general to local anesthesia, depending on the circumstances of the case (stone burden, anatomy, patient compliance). Usually, for a case of moderate-to-high complexity, general anesthesia is preferred since it allows deep muscle relaxation and best facilitates the many sorties into the kidney (up to 50 and more) that are at times required to clear a larger stone burden. General mask anesthesia, regional anesthesia, or intravenous (IV) sedation may very well be appropriate for a less-complex, shorter case. Local anesthesia with a topical anesthetic applied to the urethra may suffice for any diagnostic procedure and small-volume intrarenal pathology in the willing patient. With the exception of patients undergoing a diagnostic procedure (with low likelihood of necessary treatment) all patients are prepared for the possibility of general anesthesia, i.e. they undergo a formal preoperative clearance examination and are kept NPO after midnight (or 8 hours prior to surgery).

### *Procedure*

On the day of the planned surgery, routine patient preparation includes preoperative IV antibiotics (e.g. ampicillin and gentamicin) and a forced diuresis by IV fluids and the administration of a diuretic (10–20 mg of furosemide) once the safety wire is in place. These measures, in addition to the confirmation of sterile urine sample preoperatively, are necessary precautions to reduce the risk of infectious complications, because, during upper tract endoscopy, intrarenal pressure may increase with possible pyelorenal reflux. Reflux of infected urine into the renal parenchyma and vasculature may result in serious septic complications and the above precautions are observed to reduce the risk of reflux of irrigant.<sup>15,18</sup>

### *Access to the upper urinary tract for retrograde intrarenal surgery treatment*

The patient is positioned in the lithotomy position. RIRS can also be performed in the supine position if the lithotomy position is not feasible (leg amputation, frozen hip, morbid obesity); occasionally, RIRS is performed with the patient in the prone position as part of a combined PCNL procedure. This position will often improve lower pole access for the flexible ureteroscopy by decreasing the angle between the lower pole calyceal and renal pelvis.<sup>24,25</sup> Cystoscopy and a retrograde pyelogram to assess ureteral and intrarenal anatomy is always the initial step of RIRS. A safety wire (0.038 inch, floppy tip) is then placed up into the kidney under fluoroscopic control. The safety wire is left in place through the entire procedure when stone fragmentation is performed or when repeat access to the kidney is necessary with basket removal of stone particles (Table 30.4). In no case have we ever observed a ureteral or renal injury caused by the flexible ureterorenoscope.

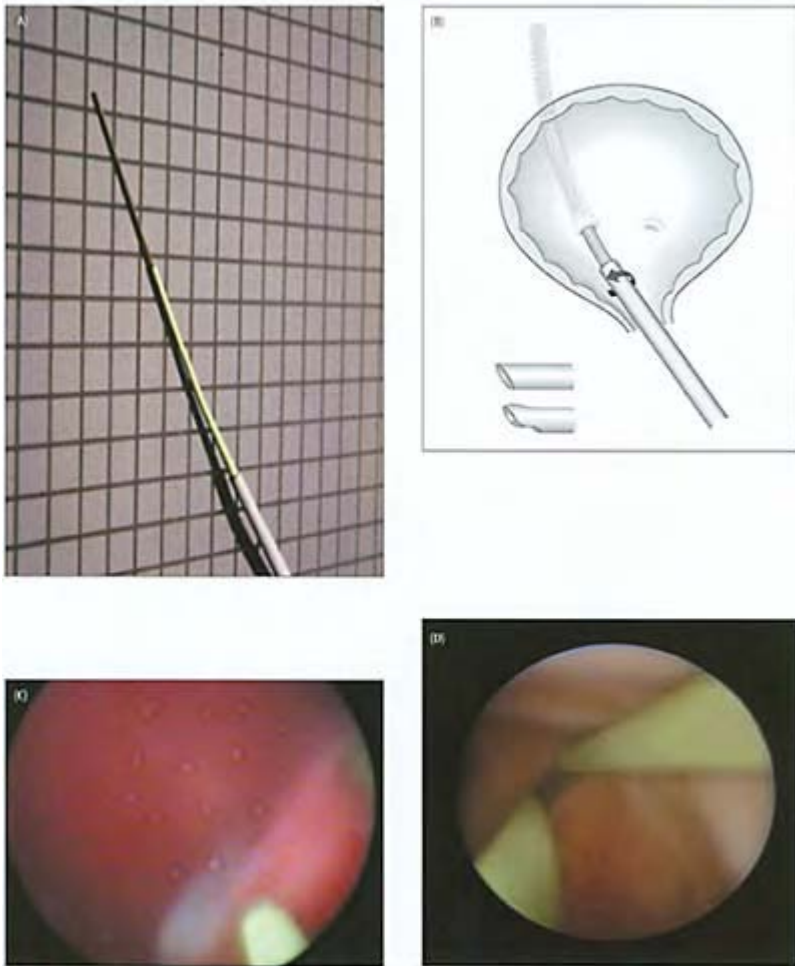
*Dilation of the ureteral orifice and/or ureteral segments*

While access with the 7.5F flexible instrument to the kidney for diagnostic evaluation is usually feasible, even under local anesthesia in the office setting, repeat access to the kidney and retrieval of stone particles from the kidney necessitate some sort of upper tract preparation. Options include serial dilators, coaxial dilators, balloon dilators, 'optical dilation', or the preparatory placement of an indwelling ureteral stent (Figures 30.3 and 30.4). Presence of an indwelling ureteral stent provides the ideal condition for upper ureteral and intrarenal access and was routinely employed in the early years of RIRS when 10.4F ureteroscopes were used.<sup>13,15</sup> Now, with the size of most flexible scopes being 6.9–7.9F, RIRS is usually performed as a onestage procedure and the authors' first choice is 'optical dilation' using a rigid 9.5F ureteroscope (Figures 30.1 and 30.4). 'Optical dilation' with a rigid 9.5F ureteroscope is the most efficient and cost-effective means of one-stage preparation of the ureteral orifice and ureter for RIRS. The 9.5F ureteroscope is introduced into the ureteral orifice over a second guide wire and advanced up the ureter as far as it can reach, thus dilating the ureteral orifice and distal two-thirds of the ureter and facilitating renal access for the 7.5F flexible ureterorenoscope (see Figure 30.4). This approach allows access to the kidney in >85% of cases in a onestage procedure. If access is not feasible in this fashion, placement of an indwelling ureteral stent is the next step. This will passively distend the entire ureter in a matter of 7–10 days and invariably facilitates intrarenal surgery, even in the presence of the need for many passages with the instruments and removal of a larger amount of gravel.<sup>13,15</sup> All other means of active dilation (serial, coaxial, or balloon dilators) are, in the authors' opinion, not ideal because of the technical difficulty and the potential for ureteral damage when multiple ureteral segments need to be dilated to gain access to the kidney and multiple

**Table 30.4** *Procedural steps of ureterorenoscopy and retrograde intrarenal surgery*

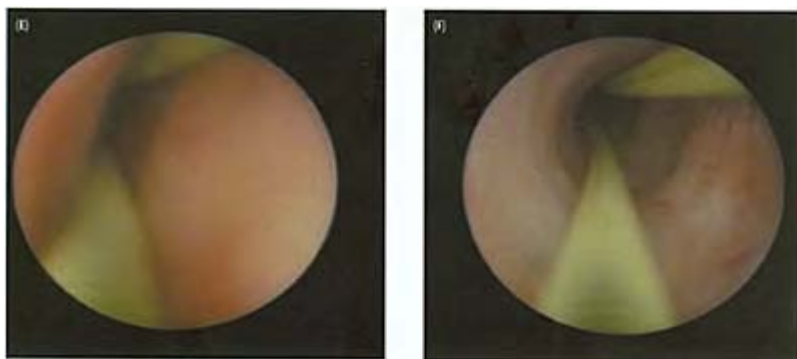
- Cystoscopy and retrograde pyelogram
  - Passage of 0.038 inch guide wire via 5F ureteral catheter (safety wire)
  - 'Optical dilation' with a 9.5F semirigid ureteroscope
  - Passage of 7.5F ureterorenoscope alongside safety wire or over second guide wire (working wire)
  - Remove working guide wire past the iliac vessels
  - Irrigation fluid is begun and the instrument is advanced under direct vision to the area of interest
  - Once the area of interest in the ureter or kidney is reached, the treatment options include:
- Stone treatment
- Remove renal stone with basket if renal collecting system is spacious or two-prong grasper if area is tight
  - Fragment impacted ureteral or renal stones too large for direct removal (EHL, laser) or when relative ureteral narrowing below stone due to edema
- EHL/laser fragmentation:
- start at low energy levels
  - clear view at all times
  - release probe when in full visual control
  - advance probe 3–4 mm beyond work channel to protect optic fibers

- Indwelling ureteral stent placed for 7–14 days
- EHL=electrohydraulic lithotripsy.



**Figure 30.4** (A) Coaxial 5 and 7F sheaths for placement of safety and working guide wires. (B) Schematic drawing of access between the guide wires for access with the 9.5F semi-rigid. (C) Endoscopic view of the 2 wire access technique with the safety wire on top and the working wire on

the bottom of the intramural ureter opening the orifice to allow access. (D) Endoscopic view of the transition from the intramural ureter to the pelvic ureter.



(E) Endoscopic view of the advancement of the rigid scope through the narrow segment (with constant pressure directed in the axis of the ureter the scope can be gradually advanced). (F) Endoscopic view of the lumen of the ureter after successful passage into the pelvic ureter.

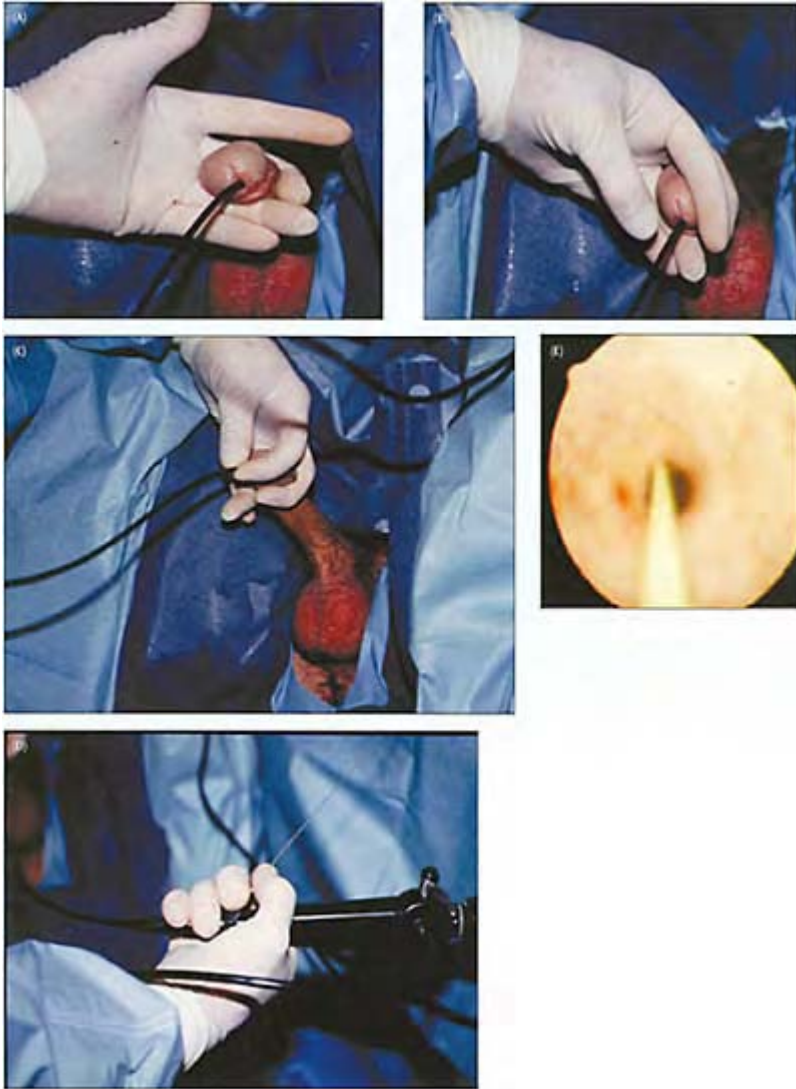
passages of stone retrieval are needed.<sup>13</sup> A detailed description of the approach to the upper urinary tract in patients with urinary diversion is given elsewhere.<sup>16</sup> In cases of a urinary conduit, it is usually possible to perform RIRS without too much attendant difficulty, whereas in cases of antirefluxive continent diversions, access to the upper tract in a retrograde fashion is rarely possible and percutaneous surgery is usually indicated.<sup>16</sup>

### *Flexible ureterorenoscopy*

Flexible upper tract instrumentation and RIRS is commonly performed with a 7.5F actively deflecting ureterorenoscope. The instrument is either advanced alongside the safety wire (most female patients or after previous stenting) or over a second 0.038 inch floppy tip 'working' guide wire (male patients or difficult access) (Figure 30.5). Specialty wires such as hydrophilic wires are usually not necessary. The instrument is advanced under direct vision (video camera) to the area of interest. During advancement of the scope, dilute contrast can be injected through the work channel to further delineate the ureteral and intrarenal anatomy. Once the area of interest in the kidney is reached, depending on the pathology found (stone, stricture, tumor, bleeding foreign body), the surgical procedure is performed. As previously alluded to, infectious and septic complications are further avoided by maintaining a low intrarenal pressure by frequent aspiration of fluid from the collecting system via the irrigation port and by using the irrigant only when needed to improve visualization (Figure 30.6). The authors strongly advise against the use of pressurized irrigant or forceful hand irrigation. Gravity irrigation

at 60 cmH<sub>2</sub>O and intermittent aspiration of fluid and/or vapor (holmium lithotripsy) is always sufficient to provide intraoperative visibility (see Figure 30.6). We utilize a three-way connector to switch between irrigation and suction (suction pump), which allows rapidly exchanging the fluid volume in the kidney and keeping pressures low (see Figure 6). If visibility remains poor, the use of a ureteral access sheath may improve visibility; otherwise, termination of the procedure with placement of an indwelling stent and return in 7–10 days is recommended in the interest of avoiding unmonitored activation of energy sources with the risk of breaching the integrity of the renal collecting system and causing bleeding and extravasation complications.

Small stone pieces of less than 4 mm size can usually be removed intact (provided the condition of the ureter accommodates unhindered withdrawal) whereas solid stones larger than 4 mm are fragmented first.<sup>26</sup> Currently, holmium laser energy is the energy source of choice for



**Figure 30.5** (A) The urethra is tightly gripped at the sulcus between fingers 3 and 4 and pulled straight. (B) While the urethra is held straight (finger 3 and 4), the scope is guided into the urethra and the ureter using finger 1 and 2 for advancement. (C) different view of the key elements in advancement of the

flexible scope in male patient. Urethra straightened using finger 3 and 4 (to avoid buckling of scope) and tip directed using finger 1 and 2 (precise maneuvering possible since 1:1 torque can be achieved). (D) Right hand action: the right hand holds the handle of the instrument with the attached video camera; also, the working wire is held at slight tension to facilitate advancement into the ureteral orifice. (E) When the scope has been advanced above the iliac vessels the working wire is removed; the endoscopic view shows that the ureter after 'optical dilation' easily accommodates passage of the scope alongside the safety wire.



**Figure 30.6** (A) Three-way connector for irrigation and intermittent suction facilitates RIRS and helps keep intrarenal pressures low. (B) Suction pump allows regulation of suction.

fragmentation and—if needed—incision of intrarenal strictures.<sup>27,28</sup> The holmium energy invariably fragments stones of all compositions and, in addition, can vaporize (debulking) stone, depending on composition (uric acid >struvite >calcium oxalate dihydrate >calcium oxalate monohydrate >cystine): 200  $\mu$ m fibers are usually used for intrarenal work and, with very few exceptions, all calyces can be reached. Energy settings are from 20 W, for large, bulky stones, to 3 W, for final comminution of small gravel. The holmium energy rapidly reduces stone bulk by a combination of vaporization and fragmentation. Vapor is readily removed by using intermittent suction (three-way suction/irrigation system). As the stone bulk is reduced, the energy is lowered so as to reduce the kinetic energy and prevent stone propulsion, which in turn decreases the fragmentation/vaporization effect on the stone. When using energy sources for fragmentation, it is important to be in constant visual contact with the stone and not to hit the mucosa, since bleeding would ensue. Bleeding, although usually minimal—we have never seen any significant bleeding (even with EHL fragmentation or in patients with coagulopathy)—will decrease visibility, and frequent aspiration and irrigation will be needed, thus slowing down the procedure.<sup>29</sup> In these situations we keep the renal collecting system somewhat distended, since the pressure of the irrigant will effectively compress small venous oozing. At any rate, significant bleeding should and can be avoided by a cautious approach. In our personal experience, early termination of a procedure secondary to bleeding (i.e. continuous bothersome oozing) may occur in less than 1% of cases; significant bleeding, resulting in drop of hematocrit and need for blood transfusion, has never occurred in 16 years and greater than 3000 cases of RIRS.

The endpoint of the fragmentation process is reduction of all stone to gravel, allowing active basket removal (up to 3–4 mm) or spontaneous passage (less than 2 mm). If a laser device is not available, the 1.6F EHL probes can be used, as we have done for 8 years prior to the advent of the holmium technology.<sup>13,15,16,20</sup> Flexible probes are now also available for the pneumatic lithotrite (Swiss Lithoclast, EMS-Boston Scientific Corp., Natick, Massachusetts). Pneumatic lithotripsy with flexible probes is an option for the renal pelvis and the upper calyces. While the holmium laser efficiently fragments all stone compositions, a few stones, such as an occasional cystine, calcium oxalate monohydrate, or brushite stone, may resist the power of EHL lithotripsy.<sup>16,18,20</sup> In these cases, we try to bring the stone to the UPJ or the proximal ureter and then use a 10.5F rigid ureteroscope with a 2.5F ultrasound wire probe or the pneumatic device (Swiss Lithoclast).<sup>18</sup> If this cannot be accomplished, a percutaneous access is established under the same anesthesia and the stone is removed in an antegrade fashion.

Retrieval of stone gravel is performed using a four-wire tipless nitinol basket or a two- or three-pronged grasper (2.0F). Before the advent of the nitinol tipless basket, a grasper was usually employed for fragments in a calyx too small to safely accommodate an opened basket of the Segura design (with a tip and potential damage of the mucosa causing cumbersome oozing). Segura baskets are utilized in a spacious calyx, in an infundibulum, in the renal pelvis, and in the ureter. The new nitinol technology and the tipless basket design actually allows for basket retrieval maneuvers even in small calyces and as a result concomitant use of graspers is very infrequent, which is a further cost reduction.<sup>26</sup> The use of access sheaths (Applied Urology, Rancho Santa Margarita, California and Cook Urology, Spencer, Indiana) facilitates rapid reaccess to the kidney and, especially with larger amount of gravel or for the less experienced, can be helpful.<sup>24</sup>



Limiting factors for the success and efficiency of the RIRS approach are the stone burden and at times the anatomy of the lower calyceal group and the presence of a tight ureter. Stone burden directly correlates with treatment time, and increasing stone size may make the retrograde approach cumbersome and potentially traumatic. Here, experience and prudence will determine how far to push and when conversion to percutaneous renal surgery is more appropriate. As a rule, all our patients with stone burden larger than 2.5 cm are consented for concomitant use of ESWL or conversion to PCNL; the latter is employed when progress is slow, especially in the presence of unfavorable intrarenal anatomy or a tight ureter preventing expeditious retrieval of gravel.

The RIRS procedure is concluded with placement of a 7F indwelling ureteral stent of appropriate length. The postoperative indwelling time is between 3 and 14 days, depending on the amount of edema, manipulation in the ureter, and residual gravel remaining in the kidney for spontaneous passage.<sup>30</sup> We use an indwelling stent with a string attached to the distal end (in male patients). The string is cut at the meatus, which in male patients allows removal by a limited urethroscopy under topical anesthesia; in the female patient, the string is removed and cystoscopy under topical anesthesia is needed. The patient is discharged the day of surgery, with an appropriate oral antibiotic for 5 days (in case of previous infection), 6 days supply of Pyridium (100 mg orally three times a day), and 10 tablets of an oral pain medication (e.g. Darvocet-N 100). The patient will return to the clinic between 3 and 14 days after surgery for an ultrasound of the kidney (r/o (renal obstruction) stone and/or hydronephrosis), a plain abdominal X-ray (if there is any doubt as to whether the ureter is stone free, based on previous amount of gravel, or if ultrasound shows hydronephrosis), and stent removal. Two weeks after stent removal, the patient returns for renal ultrasound (r/o stone or hydronephrosis) and urine is checked for bacteria. The further follow-up is individualized, depending on the clinical situation, but all patients return at the 3 months timeline to assess and record their stone-free status and kidney condition and to monitor and adjust their stone metaphylaxis.

### **Common indications for retrograde intrarenal surgery**

The most common indications for RIRS, historically and at present, are secondary treatment of retained stones after ESWL and, more specifically, stone retrieval of residual stone from the lower calyceal group. The most common primary indications for RIRS in our practice are renal stones up to 1.5 cm of known calcium oxalate monohydrate or cystine composition, and stones up to 1.5 cm in the lower calyceal group of any composition (see Tables 30.1 and 30.2).

#### *Retrograde intrarenal surgery for lower calyceal solid stones or residual*

The management options for the initial treatment of lower calyceal stones include ESWL, PCNL, RIRS, and, to a much lesser extent, open surgery.<sup>31–35</sup> ESWL is the most commonly employed initial treatment modality, with a wide range of stone-free rates (30–90%, depending on stone size, composition, and lower pole anatomy).<sup>35</sup> Frequently, lower pole stone patients are referred to an endourology subspecialty center with retained

stones after having received one or more sessions with ESWL. In this setting, RIRS is particularly beneficial because it affords the advantage of direct endoscopic stone removal with minor invasiveness as compared to PCNL (even in the 'mini-perc' version). Patients who retain stone fragments after ESWL in the lower calyceal group without a stent are usually followed conservatively with watchful waiting until they become symptomatic with pain and/or infection or regrowth of the stone to a size where spontaneous passage cannot be expected (>7 mm). If infection persists after ESWL or recurrent urinary tract infections are encountered, the rate of regrowth and risk of complications are significantly higher.<sup>34-36</sup> In the case of persisting or recurrent infection, antibiotic therapy is instituted and, once the infection is eradicated, the residual is removed using the RIRS or percutaneous technique in the case of a stone burden in excess of 2.0–2.5 cm. When ESWL fails to render a patient stone free, additional treatment may include repeat ESWL, PCNL, or RIRS. Repeat ESWL is an option, but repeating the ESWL procedure may again not be curative and the result in the individual patient is by no means predictable.<sup>34,35</sup> Of the above options, RIRS is an excellent choice for retained stones of 15 mm or less and for up to 10 particles of an individual size of 4 mm or less.<sup>33,34,36,37</sup> In these cases, RIRS is performed with holmium laser energy, since this energy will effectively fragment all stone compositions. Based on stone-free rates of >90% for RIRS treatment of retained lower calyceal stones after ESWL, RIRS has also become the authors' primary treatment choice for lower calyceal stones of <1.5 cm size (Tables 30.5 and 30.6). Stent placement is often a component of the ESWL treatment and presence of the indwelling stent leads to ureteral dilation, which this facilitates advancement of the flexible ureterorenoscope into the ureter and kidney. Therefore, if multiple fragments larger than 4 mm remain in the kidney after ESWL and a stent is indwelling, the decision to employ RIRS is best made prior to removal of the indwelling stent.<sup>34</sup>

Usually, RIRS allows direct access to the lower pole stones and treatment (fragmentation and/or stone removal) which, obviously, is the ideal scenario (Figures 30.7 and 30.8).<sup>34,36,37</sup> At times, direct access to the lower calyceal group is technically challenging or not feasible, when the renal collecting system is small or when there is a long infundibulum with an acute angle, or after previous surgery, when a distorted anatomy prevents access. Although the stone may be adequately visualized in the lower calyx, stone treatment may be hampered because an accessory instrument (grasper, basket), once advanced through the work channel of a flexible scope, tends to straighten out the ureteroscope and force it out of the lower calyceal group or move the tip of the accessory instrument just enough so that the stone cannot be successfully engaged. In the latter situation, the stone can be dislodged by careful hand irrigation and aspiration and thus repositioned into a location better suited for direct removal or fragmentation. During this maneuver, the patient is best positioned in the Trendelenburg position. We also found it helpful to use a floppy-tipped guide wire through the work channel, pass it around the stone and, with a jerking pull, dislodged the stone into a better location.

The endpoint of the RIRS treatment of such complex lower pole stones is the complete fragmentation and removal of all gravel from the lower pole location. If the stone cannot be directly accessed, displacement and relocation techniques, as described above, are employed. Often, the stone can be repositioned into a 'higher' location in the kidney with a basket, a curled guide wire, or cautious hand irrigation (Figure 30.9).<sup>38-40</sup> If this is not

feasible, simultaneous ESWL stone fragmentation can be employed with the stone in the lower calyx location.<sup>41</sup> The fragmented stone gravel can then be repositioned by the above techniques into locations from where basket retrieval can be successfully performed. If all these attempts are not immediately successful, we usually convert to the PCNL approach in the same setting (less than 3% of cases). Alternatively, ureteroscopic access to the lower pole can be attempted again after repositioning the patient in the prone position. This change in patient position will often make ureteroscopic tower pole calyceal access easier.

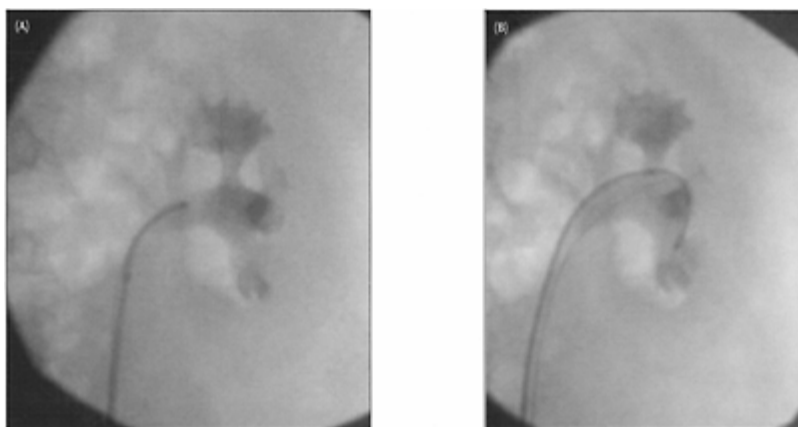
**Table 30.5** *Treatment algorithm for lower calyceal stones*

|  | SWL                                      | RIRS   | PCNL                                       |
|--|--|--|--|
| Stone size (primary)   | <1.5 cm                                  | <1.5 cm  | >1.5 cm                                    |
| Composition  | Calcium oxalate dihydrate; struvite      | Need to be stone free; all compositions                          | need to be stone free; all compositions    |
| Anatomy  | Normal                                   | Abnormal; urinary diversion; size < 1.5 cm                       | Abnormal; urinary diversion; size > 1.5 cm |
| Physiology   | Normal                                   | Abnormal; size < 1.5 cm  | Abnormal size > 1.5 cm                     |
| Residual stones (secondary)  | 5 mm and less; no stent; anesthesia-free | All sizes <1.5 cm; <10 fragments; abnormal anatomy sizes >1.5 cm | Abnormal anatomy; all                      |
| PCNL=percutaneous nephrolithotripsy; RIRS=retrograde intrarenal surgery; SWL=shock wave lithotripsy. |  |  |  |

**Table 30.6** *Comparison of treatment results of lower calyceal stones*

| Author         | Method     | Stone free | Size < 10 mm | 11–20 mm    | >20 mm                              | Auxiliary procedures |
|----------------|------------|------------|--------------|-------------|-------------------------------------|----------------------|
| McDougall      | HM-3       | 54.3%      | 63.6%        | 44.4%       | 25.0%                               | 25.0%                |
| Lingeman       | HM-3       | 72.7%      | 79.8%        | 58.2%       | 31.6%                               | 9.8%                 |
| Psihramis      | Lithostar  | 53.0%      | 60.5%        | 47.6%       | 33.3%                               | 18.6%                |
| Netto          | Lithostar  | 79.2%      | 77.7%        | 84.6%       | 50.0%                               | 41.6%                |
| Netto          | PCNL       | 95.6%      | 100%         | 93.3%       | 100%                                |                      |
| McDougall      | PCNL       | 86.2%      | 100%         | 66.6%       | 85.7%                               | 53%                  |
| Bierkens et al | Lithostar  | 36%        |              |             |                                     | 43%                  |
|                | HM-4       | 40%        |              |             |                                     | 32%                  |
|                | Piezolith  | 48%        |              |             |                                     | 59%                  |
|                | Direx      | 44%        |              |             |                                     | 40%                  |
|                | Breakstone | 46%        |              |             |                                     | 43%                  |
|                |            |            | Size <15 mm  | Size >15 mm |                                     |                      |
| Fuchs          | RIRS       | 93.0%      | 93.0%        |             | 85% stent, 5% PCNL, 10% 2nd session |                      |
|                | PCNL       | 96.0%      | 100%         | 92.0%       |                                     |                      |

PCNL=percutaneous nephrolithotripsy; RIRS=retrograde intrarenal surgery.



**Figure 30.7** Forty-two-year-old male with 1.0 cm and 1.2 cm lower pole stones electing RIRS treatment. (A) The scope can not be readily advanced into the stone-bearing lowermost calyx. (B) The scope has been advanced into the lower pole over a separate guide-wire; the guidewire can be removed now (leaving the safety wire in place) and a Nitinol basket can be advanced for stone retrieval. Note that safe (for the instrument channel) advancement of a 200  $\mu$ m Laser fiber may not be possible due to the extreme deflection.

*Retrograde intrarenal surgery for primary treatment of renal stones of 1.5 cm and less*

Renal stones up to 1.5 cm in size, of any location within the collecting system, can be very effectively treated with RIRS in a minimally invasive outpatient procedure. Therefore, this is one of the options we present to our patients as an alternative to ESWL, especially for patients with a known stone analysis of COMH, cystine, or uric acid, patients who need to be free of stones (pilots, infection stones), and stones associated with intrarenal stenosis (see below and Tables 30.1 and 30.2). RIRS is the ideal treatment, since it combines a high success rate (80–90+% stone free) with lesser invasiveness than PCNL. The technique is as described above, with treatment times ranging between 45 and 60 min for most cases.<sup>15,18</sup> The advantage of RIRS over ESWL is

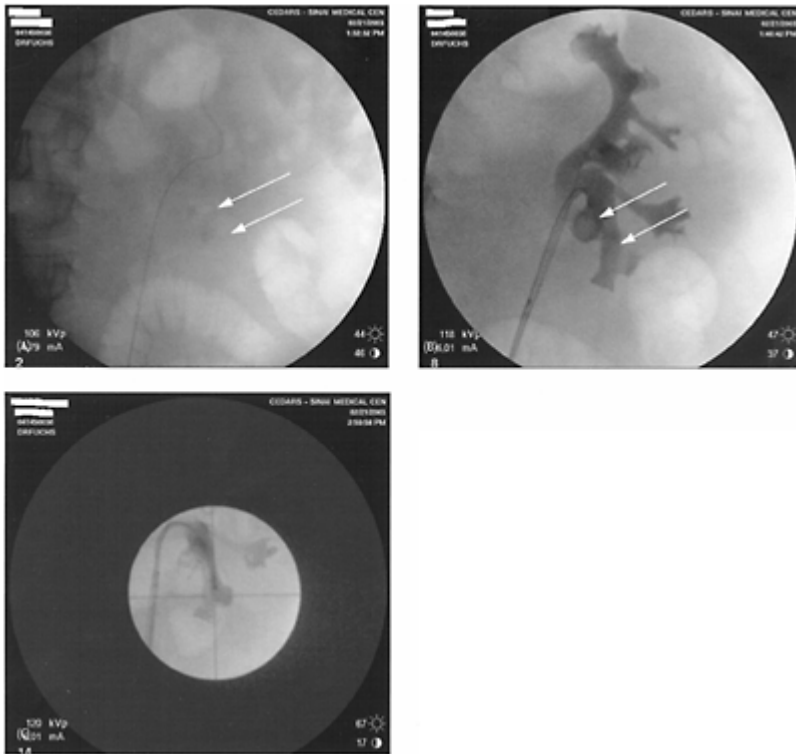
the predictability of the treatment outcome. Access to the kidney in a one-stage fashion is possible in greater than 95% of cases. Further, RIRS with holmium lithotripsy will:

1. fragment (and vaporize) the ESWL 'problem stones' very efficiently
2. the endpoint of fragmentation is endoscopically determined and not guessed from a fluoroscopic image, as in ESWL
3. active stone retrieval with baskets or graspers is part of the procedure and leaves only minute residual gravel for spontaneous passage (see also segment on RIRS-SWL) and Figure 30.8.

*Retrograde intrarenal surgery and simultaneous extracorporeal shock wave lithotripsy for the management of a larger renal stone burden*

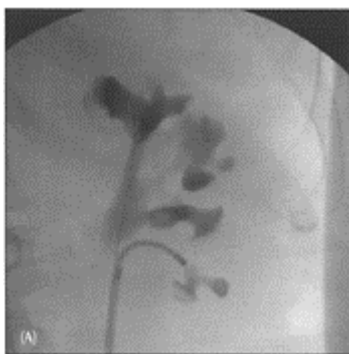
The combination of RIRS and ESWL can be employed for

1. treatment of a renal stone burden too large for either treatment modality alone ( $>1.5$  cm,  $<2.5$  cm) and not quite large enough to warrant the increased invasiveness of PCNL ( $>2.5$  cm)



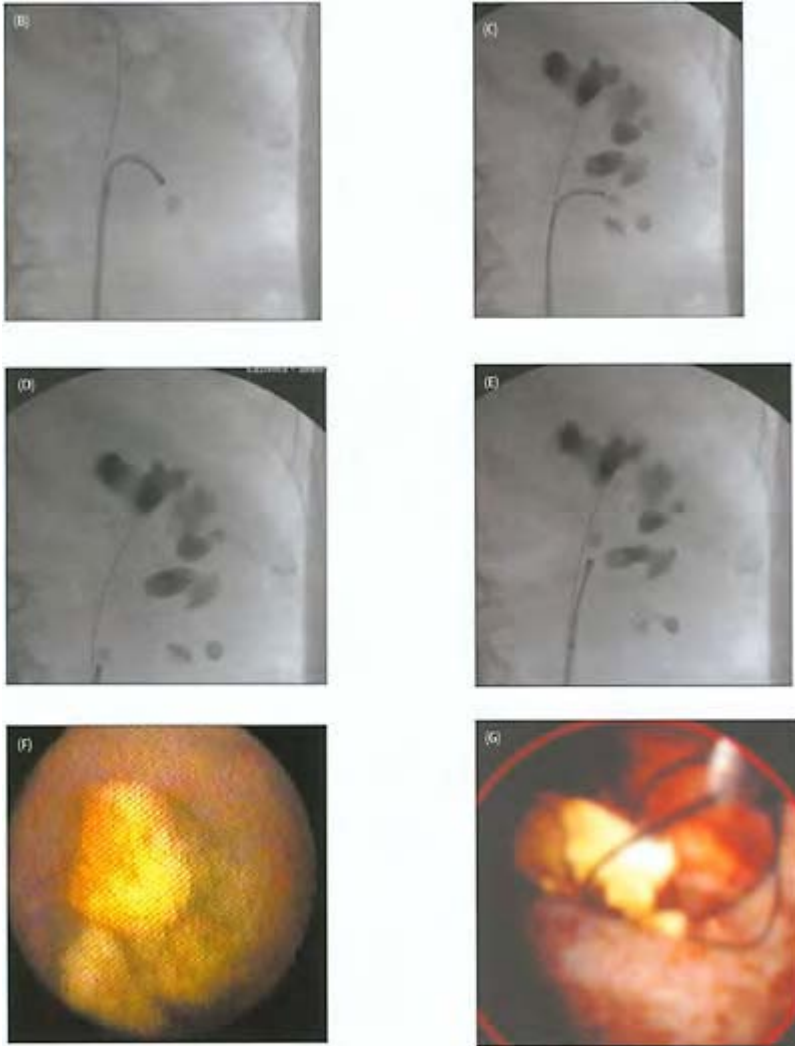
**Figure 30.8** Forty-two-year-old male with 1.0 cm and 1.2 cm lower pole

stones electing RIRS treatment. (A) KUB shows the 2 stones with safety wire in place. (B) Retrograde pyelogram with the 7.5F instrument in position for RIRS of the first lower pole stone. Note that the new instrument design (Storz FlexX, Culver City, CA) supports the rather acute angle to enter this lower calyx even with a 200 urn fiber advanced through the work channel. (C) While the first stone is treated with RIRS holmium lithotripsy, the lowermost stone is simultaneously treated with E-SWL (Storz Modulith XL); inter-mittently the endoscope is passed into the lowermost calyx to monitor the progress and determine the end point of the fragmentation (stone gravel is then actively removed and the lower calyx cleared as much as feasible). To prevent damage to the tip of the scope SWL energy is not employed while the scope is directly in the blast path.



**Figure 30.9** Lower pole stone (1.2 cm, COMH); RIRS repositioning technique. (A) Stone is readily

approached in lower calyx with 7.5F instrument.



(B) With Laser fiber (200  $\mu\text{m}$ ) in place only partial stone access is possible. (C) Stone is captured in Nitinol basket for repositioning into higher renal location. (D) Stone is withdrawn into renal pelvis and then advanced to upper pole infundibulum for holmium laser fragmentation. (E, F, G) Stone is securely wedged in the upper pole infundibulum and fragmented/vaporized with Holmium energy (10–3 W); all resultant gravel larger than 2 mm is actively removed.

2. when RIRS cannot reach all stone for successful fragmentation, such as impacted lower calyceal stone or other intrarenal location dependent on the axis of the access infundibulum.<sup>41</sup>

The treatment goal is the complete fragmentation/vaporization of the renal stone burden and removal of gravel to the point where the amount of residual is small enough so that spontaneous passage can be expected (Figure 30.10A and B). The procedure is performed on a multipurpose endourologic table equipped with an ESWL energy source (authors' personal experience with Dornier MFL 5000, Direx, and Storz Modulith XL). Basically, the treatment starts as a regular RIRS, with fragmentation and vaporization of the most central stone burden. Once the central stone portion has been cleared, ESWL is employed for the peripheral stone burden (especially the lower and mid calyces) and RIRS continues to treat the upper pole calyces (see Figure 30.10). The reason for the staggered deployment of ESWL is the fact that ESWL, unlike holmium laser energy, generates mild parenchymal bleeding that decreases visibility and may slow down the RIRS process. A frequent question is whether the ESWL energy can damage the flexible ureterorenoscope. Having employed this technique since 1995 on several hundred patients, the authors can attest to the safety of this approach, both for the patient and the endoscopic instruments. Initially, RIRS-monitored ESWL was performed on a Dornier MFL 5000 lithotripter using the Storz 10.4F ureterorenoscope. The reason for monitoring the SWL action was the inferior fragmentation performance of the MFL 5000 compared with the previously used Dornier HM-3 lithotripter. RIRS monitoring was performed on patients having failed ESWL treatment and established the fact that focusing precisely and keeping the stone in the (smaller) blast path of the MFL 5000 was critical to fragmentation. RIRS monitoring also established that energy levels below 25 kV did not result in stone comminution (in adult patients). While the tip of the scope was not voluntarily placed in the focal zone, renal movement with breathing excursion naturally would lead to shock wave exposure of the scope. This intermittent exposure would not result in damage of a previously undamaged scope, whereas scopes with previous damage of bundles occasionally would show more breakage of fibers with repeat exposure. Over time the technique has been modified and the ureteroscope is not directly exposed to shock wave energy to address concerns about potential damage. There is no added benefit from having the scope in the focal zone with any of the three basic RIRS-SWL techniques (monitoring of ESWL progress, localization of radiolucent stones for ESWL, and RIRS-assisted ESWL). In all three techniques the scope can be kept out of potential harms way by withdrawing to a safe 'observation post' monitoring or localizing (scope needs to be in contact with the stone only until the stone is localized fluoroscopically) radiolucent stone—or during RIRS-SWL when different areas of the kidney are treated simultaneously with RIRS or ESWL. At any rate, before engaging in the RIRS-SWL procedure, urologists may want to check with the manufacturers of their equipment (lithotripter and endoscopes) so as to not be burdened with potential liability issues at a later point.

Active stone removal is an integral part of the combined approach and in this setting we frequently use a ureteral access sheath to accelerate stone retrieval. The endpoint of stone fragmentation (gravel reduced to 2 mm or less) intrarenal and extracorporeal—can be readily assessed with the flexible ureterorenoscope. When multiple calyceal stones are encountered (without renal pelvic stone burden), treatment starts simultaneously with



RIRS in the upper/mid renal area and ESWL concentrating on the lower pole with intermittent endoscopic monitoring of the ESWL progress. The combined approach is usually an outpatient procedure and the stone-free rate for a group of 45 patients with an average stone size of 2.4 cm was 84%.<sup>41</sup>

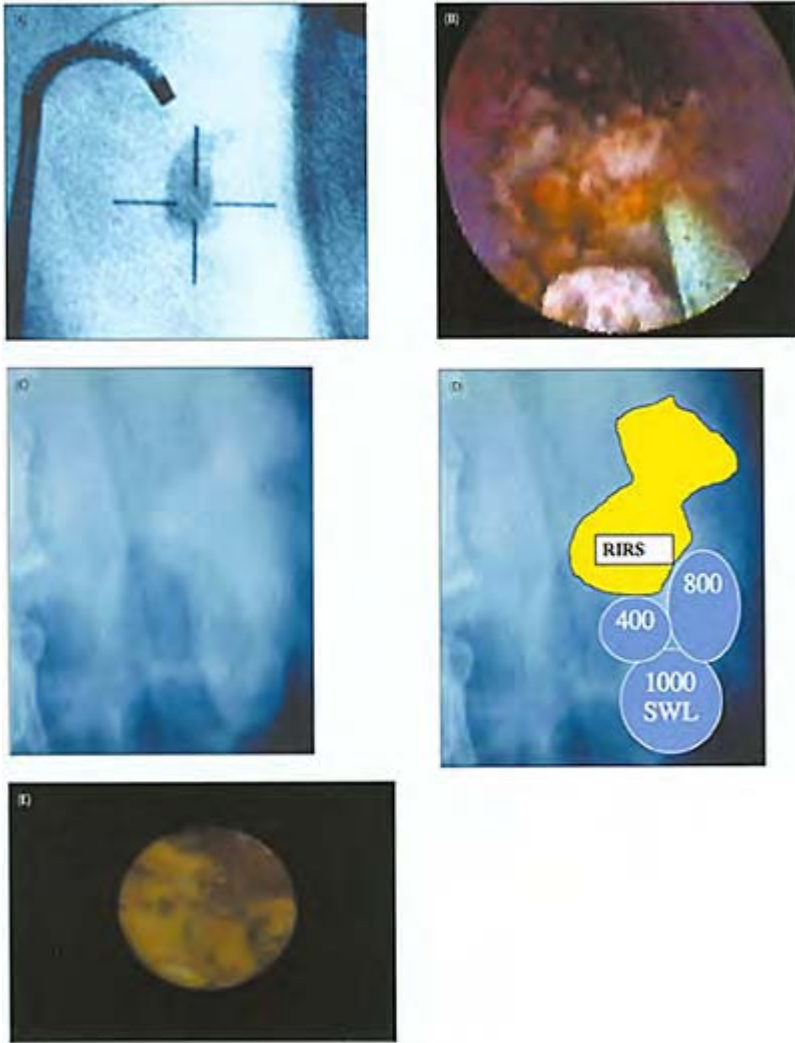
### **Special indications for retrograde intrarenal surgery**

#### *Retrograde intrarenal surgery for stones and intrarenal stenosis, including calyceal diverticuli*

Successful ESWL treatment consists of two main elements: the sufficient stone comminution and the unhindered passage of gravel from the urinary tract.<sup>1–3</sup> Although commonly employed, ESWL treatment of stones in calyceal diverticuli has a low rate of stone-free status (4–25%).<sup>42–44</sup> Psirahmis and Dretler reported a stone-free rate of only 20%, but found 75% of patients free of pain during short-term follow-up.<sup>42</sup> Lingeman reported only 4% (1 in 26) stone free and 36% of patients symptom free after ESWL monotherapy. In contrast, of 14 patients treated with percutaneous surgery alone, 13 became stone free (96%) and of the 26 patients treated initially with ESWL, 10 required percutaneous surgery to render them stone free and relieve their symptoms.<sup>45</sup>

In the best-case scenario, selecting patients with a radiographically patent calyceal neck and small stone burden of 7.9 mm, Stroom and Yost achieved a stone-free rate of 58% and 86% of patients were symptom free.<sup>46</sup>

Our personal experience with stones in calyceal diverticuli confirms both: the poor results with ESWL (43% stone free, including second ESWL sessions) and an over 90% success rate that can be achieved with percutaneous surgery. Because of the poor ESWL results and the often rather high invasiveness of percutaneous surgery for a



**Figure 30.10** Solid lower pole stone, previous E-SWL twice. (A) RIRS is being performed on the proximal portion of the stone while the dis-tal portion is positioned in the cross-hairs of the E-SWL lithotripter.

(B) Endpoint of the procedure shows complete fragmentation to size <2 mm

as compared to size of the 1 mm guide-wire.

(C) Uric acid complete staghorn stone (with contrast). (D) Treatment plan for RIRS-SWL of complete staghorn stone.

(E) Endpoint of complete fragmentation and vaporization.

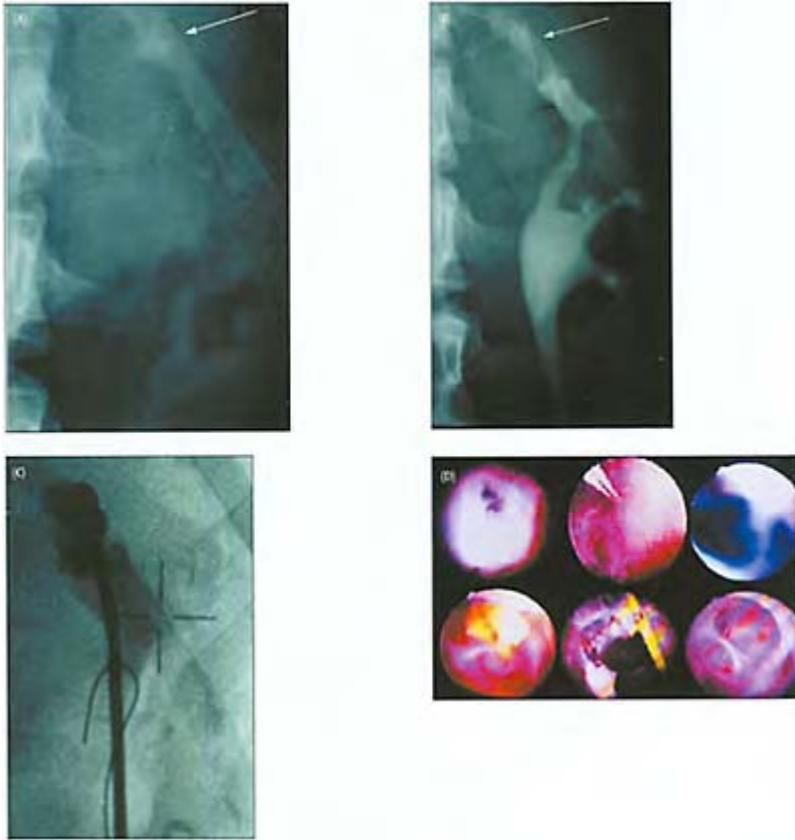
small stone in a diverticulum, we started using RIRS for selected patients in 1986.<sup>13</sup> The RIRS treatment approach consists of flexible ureterorenoscopy to identify the narrow calyceal neck, placement of a coiled guide wire into the diverticulum, repair of the narrow neck, and treatment/ removal of the stone (Figure 30.11). The results are comparable to percutaneous surgery for patients with diverticuli in the upper pole and in the mid renal region, whereas diverticuli in the lower pole at times cannot be treated in this fashion. Accordingly, since 1987, RIRS has been the approach of first choice in all appropriate patients with intrarenal stenosis. In patients with stones in the upper or mid calyceal group suspected of being located in calyceal diverticuli or trapped behind long, narrow calyceal necks, we first perform a cystoscopy and retrograde pyelogram studies to determine the best treatment approach. If no clearly patent connection to the stone-bearing calyx is seen on a retrograde contrast study, flexible ureterorenoscopy is performed for endoscopic inspection of the renal collecting system.<sup>13,47</sup> Ureterorenoscopy is performed by passing the ureterorenoscope alongside or over the guide wire (after optical dilation; see above under Basic techniques of retrograde intrarenal surgery). When the instrument is passed over the guide wire, the wire is removed once the ureterscope is in the proximal ureter, irrigation fluid is begun, and the instrument is advanced under direct vision to the area of interest. Note that we do not advance the guide wire into the kidney before endoscopic evaluation of the collecting system so as to not cause marks that could be confused with the small dimple usually seen at the entrance of the narrow segment.<sup>13,47</sup> Once in the kidney, dilute contrast is again injected through the scope to fluoroscopically delineate the connection to the stone-bearing calyx if possible. This will further narrow down the area of interest and usually a small dimple can be endoscopically identified, indicating the entry to the narrow intrarenal segment (see Figure 30.1 1D). A 0.038 inch Bentson-type guide wire is then inserted and maneuvered into the narrow segment under fluoroscopic guidance; if this wire does not pass, a hydrophilic glide wire can be tried next. Once a wire connection is established, the scope is removed and a 5F straight angiocatheter is passed over the wire and through the narrow segment for initial dilation; if a glide wire was used, this is exchanged now for a regular Bentson-type wire.

For reconstruction of the narrow segment three different procedures are employed, depending on the length of the narrow segment and whether or not a wire can be placed into the cavity to identify and secure access. If the infundibulum is short (<0.5 cm), the obstruction can often be negotiated with advancement of the 7.5F scope over a second guide wire (see Figure 30.11). A longer (>0.5 cm to 1.5 cm) segment is best managed with balloon dilation. A zero-tip 3F balloon (dilation to 14F) is advanced over the guide

wire and inflated under fluoroscopic control. A laser incision is usually performed subsequently to open the lumen sufficiently after the initial instrument or balloon dilation has negotiated access into the cavity. Holmium laser technology is ideally suited for this purpose. The shallow depth of penetration (0.4 mm) allows for precise incision along the previously dilated segment. The direction of incision is selected towards the posterior aspect of the segment to avoid the vascularity of the anterior aspect of the infundibulum. The energy chosen is 10 W (1 Joule at 10 Hz). At times, no access can be identified, but the diverticulum bulges into the collecting system like an obstructing parapelvic cyst, in which case a laser incision (holmium 10 W) is appropriate to widely marsupialize the cavity into the collecting system. In cases where no access can be endoscopically identified but the cavity fills with contrast, the 'Blue Spritz' technique can be helpful. Methylene blue is injected through the work channel and, like the contrast, it will find its way into the cavity. Then the collecting system is washed clear of the blue dye and, under low-pressure conditions, and with the scope scanning the area of interest, a trickle of blue coming from the cavity will lead to the entry and allow successful negotiation (see Figure 30.1 1D).

After access is gained, use either direct removal of the stone (for a small stone less than 4 mm, the calyx is spacious enough to allow for basket or three-prong grasper manipulation), or fragmentation of a stone slightly too large for direct removal using laser (holmium, Lumenis) energy. An electrohydraulic lithotripter (Calcutript, Karl Storz, Culver City, California) or the use of the flexible pneumatic probes (Swiss LithoClast, EMS-Boston Scientific Corp., Natick, Massachusetts; for upper pole use only) are options when a laser is not available. For larger or multiple stones, ESWL can be performed under the same anesthesia to accelerate and complete fragmentation.<sup>41,47</sup> Stone gravel is actively removed from the upper tract with baskets, and the small gravel (<2 mm) is left for spontaneous passage. The endpoint of the treatment is the 'repair' of the narrow segment and the complete removal of all stone from the diverticulum/cavity. A small amount of gravel outside the target cavity can be 'tolerated' and will pass much like in other intrarenal stone treatments. At the conclusion of the treatment, an indwelling stent is placed. The stent is preferentially placed into the target calyx if space permits since this will, in our assessment, improve the healing of the incised segment.<sup>13,47</sup>

ESWL, when applicable, in our initial series was performed in the standard fashion using the unmodified Dornier HM3 lithotripter. This process was rather cumbersome since it necessitated moving the patient from the endoscopy table to the lithotripter and at times back to the endoscopy table for fragment retrieval and placement of the stent. Now, over the last 8 years, we have performed ESWL (Dornier MFL 5000, Direx, Storz Modulith XL



**Figure 30.11** Upper pole diverticulum with stones and recurrent infection; s/p SWL three times.) (A) KUB shows well fragmented of gravel overlying upper pole of kidney. (B) On retrograde pyelogram a small amount of contrast is visualized in the diverticulum; therefore the 'Bluespritz' technique is used to aid in identification of the access to the diverticulum. (C) The infundibulum has been widely incised and the fragments removed; the contrast study (with the 7.5F instrument in the diverticulum) shows the extent of the

cavity and free contrast flow into the collecting system. (D) From left to right, top row: 1. access dimple into infundibulum after initial dilation with guide wire and 5F angiocatheter; 2. Holmium laser incision (200  $\mu$ m, 10 W); 3. the infundibulum is widely incised and the methylene blue is draining out. Bottom row: 4. well fragmented stone gravel in the diverticulum is removed with zero-tip basket; 5. the infundibulum is fully patent; 6. the diverticulum has been cleaned of all stone gravel. Picture series: Retained mid renal stones s/p 2  $\times$ SWL treatment (aviation pilot).

multipurpose lithotriptors) under direct ureteroscopic control of the fragmentation and removed stone fragments during the procedure to decrease stone passage time and improve stone clearance rates.

The stent is usually left indwelling for 2–3 weeks when the diverticulum is spacious enough to accept the proximal curl; otherwise, the stent is removed at the time of regular follow-up (2 weeks) when the patient is completely stone free or no fragments remain requiring further treatment or pose a potential risk of ureteral obstruction. Of 96 patients treated with RIRS between 1986 and 1996, 67 (70%) had an upper pole, 22 (23%) a mid pole diverticulum, and 7 (7%) a lower pole diverticulum. Of these 96 patients, the calyceal neck could be identified and dilated in 91 (95%). In 4 patients with lower pole diverticuli, the calyceal neck could not be dilated, in 2 due to the inability to place the balloon catheter. If a lower pole diverticulum cannot be successfully treated with RIRS, percutaneous surgery is performed under the same anesthesia. If the cavity in the dependent lower pole location is larger than 2.0 cm, a primary percutaneous surgery is performed. In 60 of the 91 patients in whom dilation of the calyceal neck was accomplished, the stone could be either removed intact with a 3F grasper or balloon (20 patients) or was fragmented with an electrohydraulic or holmium laser probe (10 patients). The endoscopic stone-free rates in these two groups were 94% and 90%, respectively. Seventeen patients with larger stone burdens (larger than 1.5 cm) underwent RIRS and subsequent ESWL fragmentation. In the last 5 patients, ESWL was performed under direct RIRS control on a Dornier MFL 5000 multifunctional lithotripter and stone fragments were removed during the ESWL procedure. The stone-free rate in the 12 patients receiving RIRS followed by ESWL under the same anesthesia was 75%, whereas all 5 patients in the RIRS-assisted ESWL group became stone free.<sup>48</sup>

Based on these results, our present approach to stones contained in calyceal diverticuli is as follows. In the light of poor success with the ESWL monotherapy, and the increased

rate of complications with the PCNL treatment of stones in calyceal diverticuli, our approach of endoscopic intrarenal correction of the outflow alteration, followed by ESWL when necessary, is an effective alternative. Upper pole and mid renal diverticuli are primarily addressed with the RIRS approach. Diverticuli with a long narrow segment (>1.5 cm) and those with a larger cavity (>2.0 cm) in a dependent location relative to the infundibulum, lower pole diverticuli larger than 2.0 cm, and diverticuli having failed RIRS treatment are primarily treated with percutaneous surgery. In our institution, ESWL is never employed as a monotherapy, although there remains a role for ESWL in combination with simultaneous RIRS for stone burdens too large for RIRS monotherapy but not quite large enough for PCNL (>1.5 cm and <2.5 cm).<sup>41,47,48</sup> Overall, retrograde endoscopic repair and stone removal yields a 95% stonefree rate for the diverticuli, whereas the renal stone-free rate for RIRS monotherapy is 85%, and, for the combined RIRS-SWL, 75% of kidneys became completely stone free.<sup>44</sup> Only 10, i.e. 11% of patients had a recurrence over a mean 6.4-year observation period.

Our experience confirms that this treatment algorithm compares favorably to percutaneous renal surgery with regard to stone-free rates, long-term resolution of symptoms, restenosis of the calyceal neck, and stone recurrence rates.

Laparoscopic surgery is employed in the occasional patient with a 'blown-out' calyceal diverticulum without overlying parenchyma, especially when associated with:

1. a large stone burden
2. a larger diverticulum in dependent location with regard to the infundibulum
3. either of the previous settings, being located anteriorly in the kidney.<sup>48</sup>

#### *Retrograde intrarenal surgery for the management of stones in the solitary kidney*

In patients with stones in a solitary kidney the treatment goal is to achieve a stone-free state, and to preserve the valuable remaining functioning parenchyma.<sup>48-50</sup> Accordingly, modern treatment strategies for stones in a solitary kidney are tailored to reduce the risk of ureteral stone obstruction and to maintain patency of the single ureter. Kidney stones of 5 mm or less in maximum diameter, with unimpaired drainage to the bladder, are monitored for spontaneous passage. Once a stone has migrated into the ureter, prudence dictates that such patients need to be followed at close intervals using renal sonography in combination with abdominal radiography for opaque stones. Naturally, the patient is alerted to keep an eye on urine output and report to the urologist in the event of oligouria or anuria, regardless of being symptomatic or not.

Stones of 5–10 mm in maximum dimension may still pass spontaneously but the risk of ureteral obstruction is higher. Elective shock wave lithotripsy remains the treatment of choice here unless stone composition is COMH, cystine, or uric acid (see above). If ESWL is chosen, regular evaluation, as indicated above, is essential and an indwelling stent should be placed to protect ureteral patency.<sup>48,51</sup> RIRS is a valuable treatment alternative in the setting of a solitary kidney since this technique reliably fragments all stones and removes gravel, thereby reducing the risk of ureteral obstruction.<sup>48</sup> In order to preserve renal functions in a solitary kidney, many urologists consider RIRS as the primary treatment for renal calculi in a solitary kidney.

Stone burden larger than 2.0 cm and staghorn stones in the solitary kidney are best treated by percutaneous nephrolithotomy; RIRS, as a monotherapy or in combination with ESWL, is a valuable alternative in select patients when a PCNL is not feasible or deemed too risky.<sup>48</sup>

*Retrograde intrarenal surgery for the management of stones in transplant and pelvic kidneys*

Stones in a transplanted kidney are a special form of a solitary kidney scenario.<sup>52</sup> In addition to the solitary kidney status, standard ESWL is more difficult because of the pelvic kidney location and the potential technical difficulty of intervention for ureteral obstruction in the transplanted ureter. From a technical standpoint, transplant kidneys and pelvic kidneys share the difficulty of positioning the patient in a way that allows fluoroscopic stone localization, exposure of the stone to the shock wave without energy absorption by bony structures, and fluoroscopic assessment of stone fragmentation.<sup>53</sup> Often the patient needs to be positioned in the prone position so that the stone can be exposed to the shock waves without attenuation by bony structures.<sup>48,53</sup> A second concern is the transport capacity of the ureter and the solitary kidney situation (transplant kidney) as well as the technical difficulty of accessing the ureteral anastomosis in a retrograde fashion should the ureter become obstructed by stone material (transplant kidney). These patients need to be very carefully monitored in terms of decreasing urine output and development of hydronephrosis. In terms of selection of the appropriate treatment modality, we follow the same approach as for the solitary kidney in normotopic location.<sup>48,52</sup> In stones of a size larger than 1.0 cm, an indwelling ureteral stent is placed to reduce the risk of ureteral obstruction and anuria. In the transplant kidney, the additional rationale is the difficulty of catheterizing the implanted ureter. Placement of a ureteral stent is much rather done as part of the original procedure than when necessitated by an obstructive complication. Stones larger than 2 cm are best treated using a percutaneous approach. This will render the patient stone free in an expeditious and still only minimally invasive way.<sup>48</sup> If a stone cannot be well visualized (small and/or radiolucent) or if there is an intrarenal stenosis present, we prefer endoscopic surgery as the first choice. Stones associated with anatomic abnormalities (strictures, caliectasis), and smaller than 1.5 cm, can undergo RIRS as the treatment of choice; larger stones are approached with percutaneous surgery.<sup>48</sup> In conclusion, in our experience, stones in transplant and pelvic kidneys can be treated safely and effectively using ESWL and, more commonly, endourologic techniques. With the advent of laparoscopic urologic surgery, some of the larger stones, namely those located in the renal pelvis (> 2.0 cm), may very well be approached using the laparoscope.

*Retrograde intrarenal surgery for renal stones and nephrocalcinosis*

ESWL has been the treatment of choice in patients with renal tubular acidosis (RTA) and nephrocalcinosis. Success with ESWL is hampered by the inability to fluoroscopically differentiate stones in the renal collecting system from renal parenchymal calcifications. This dilemma has led to renal overexposure to shock wave energy in patients having stone symptoms in the presence of RTA or nephrocalcinosis.<sup>54-56</sup>



In our practice, we utilize flexible upper tract endoscopy for selective evaluation of the intrarenal collecting system to determine the proper treatment approach. Endoscopically, easy identification of stones in the renal collecting system and submucosal calcifications can differentiate those from parenchymal calcifications. The evaluation is protocolized on the preoperative retrograde pyelogram film and, once localized to the renal collecting system, the stones are treated with RIRS. Likewise, larger stones can be treated with the combination of RIRS and ESWL or by percutaneous removal.<sup>48</sup> This approach has significantly reduced the use of ESWL and the amount of energy delivered per ESWL session since treatment is only performed once the stone is proven to be within the renal collecting system, thereby avoiding unnecessary treatment of submucosal and intraparenchymal calcifications.

Although ESWL may successfully treat an obstructing stone, there appears to be no role in the management of a renal stone burden or prophylaxis of future stone events since intraparenchymal calcifications cannot be distinguished radiographically from the potentially harmful calcifications in the collecting system (stones). This leads to overexposure of the kidney to the shock wave energy and poor results. Over the past 12 years no patients with medullary sponge kidney (MSK), RTA, or nephrocalcinosis has undergone a primary ESWL procedure at our institution, and RIRS has assumed the main role in the interventional management of these complex renal stone conditions. Of 22 patients treated over the past 8 years (since the introduction of holmium), 14 were managed with retrograde intrarenal ureteroscopic surgery alone, simultaneous RIRS and SWL was performed in 3 patients on a Dornier MFL 5000 lithotripter and in 2 on a Storz Modulith XL, and in 3 cases percutaneous surgery was performed to address a larger stone burden.<sup>48</sup>

*Retrograde intrarenal surgery for management of urinary tract stones in the patient with urinary diversion*

Stones are a common complication of a urinary conduit type diversion, usually secondary to recurrent infection and reflux of infected urine.<sup>48,57</sup> ESWL is of limited benefit because of poor stone opacification and, frequently, abundant gas overlying the renal shadow. The retrograde route of access generally precludes the use of rigid instruments. With the patient in the supine position, the conduit can usually be navigated with a flexible cystoscope. Conduit tortuosity can be negotiated by outlining the way ahead by contrast and fluoroscopy as well as the use of a 5F angiocatheter and guide wire to provide the necessary fulcrum and guidance for advancing the scope. Most urologists have found it difficult to identify the ureterointestinal anastomosis by retrograde endoscopic imaging.<sup>58</sup> Prior knowledge of the implantation method (Bricker or Wallace) and location of the entry into the conduit will facilitate the necessary search for the anastomosis. The difficulties of access to the ureter can be overcome by evacuation of all mucus, followed by a careful search for sessile well-circumscribed areas that resemble granulation in the wall of the urinary reservoir. Such areas are then gently probed with a floppy-tipped guide wire or a glide wire. Passage of a guide wire up one ureter is often helpful in locating the contralateral ureter, particularly in the case of a Wallace-type anastomosis. Also, placement of a guide wire into one upper tract will stabilize the conduit and thereby facilitate the search for the second site of implantation.<sup>48</sup> If the ureterointestinal

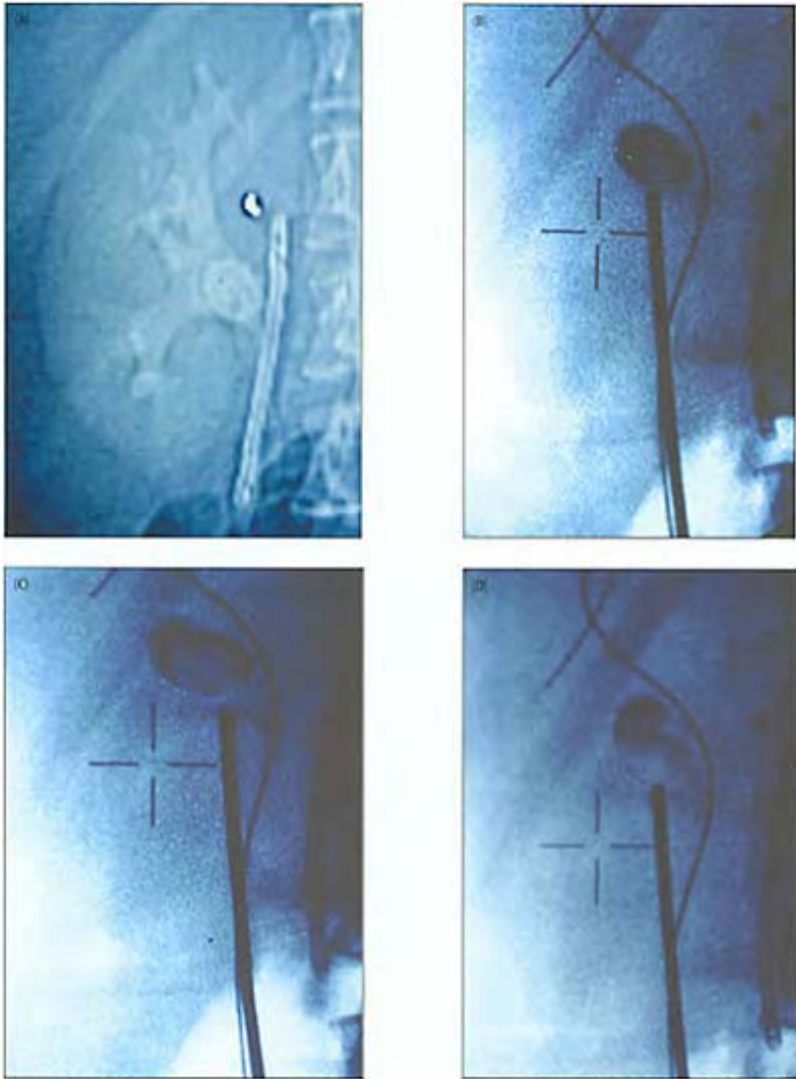
anastomosis cannot be visually identified, an IV injection of methylene blue may be of additional help in identifying the entry of the ureters into the conduit. Once the anastomosis has been identified and cannulated with a safety wire preloaded in a 5F angiocatheter, the wire is advanced under fluoroscopic control and coiled into the kidney before the angiocatheter is advanced up the ureter to gently dilate the ureteral orifice. After passage of the angiocatheter over the working wire, the working wire can be temporarily removed and a retrograde pyelogram is performed to define the anatomy of the upper tract before passage of the flexible ureteroscope. A coaxial set is then used to place a second wire, which serves as a working wire. The working wire is used to tent open the ureteral anastomosis so that the endoscope may then be passed between the two wires. If space in the ureter permits, we use an access sheath to facilitate reaccess to the upper tract. RIRS treatment in the kidney follows the principles previously described in this chapter.

### *Retrograde intra renal surgery for patients with coagulopathy*

When coagulopathy or the medical need for anticoagulation precludes the use of ESWL or PCNL, RIRS is the treatment of choice. In the RIRS procedure, the energy for stone fragmentation is directly applied to the stone and therefore the risk of bleeding is minimized.<sup>16,29</sup> In our practice, patients are frequently referred specifically for the treatment of renal stones in a setting of increased risk of bleeding secondary to their medical condition causing a coagulopathy (liver failure, end-stage renal failure, clotting factor deficiency) or their condition requiring anticoagulation (cardiac arrhythmia, transient ischemic attack (TIA) or stroke, risk of thromboembolic complications). If in the assessment of the patient's physician (cardiologist, neurologist, etc.) a coagulopathy cannot be corrected or anticoagulation cannot be discontinued perioperatively, RIRS is performed for the management of renal stones with the understanding that it is the treatment modality with the lowest risk for bleeding complications (Figure 30.12). It is our routine in these patients to utilize an access sheath, since this will 'protect' the access—especially the male prostatic urethra—and thereby reduce the risk of bleeding associated with multiple passages of the instrument. Holmium is the energy source of choice since its energy delivery is the most precise, with the least spread of energy and therefore the lowest risk of causing cumbersome bleeding.

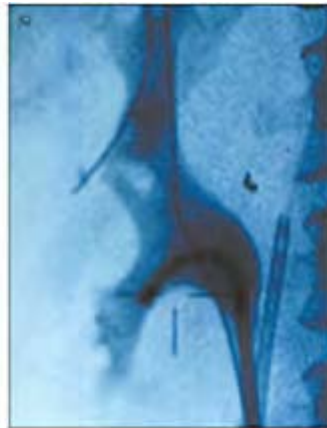
### *Retrograde intra renal surgery for the morbidly obese patient*

In the morbidly obese patient with kidney stones, access to the stone location within the kidney is not possible for ESWL, and PCNL may also not reach.<sup>59</sup> Such cases can be treated with RIRS using the aforementioned techniques. At times, patient weight even exceeds the weight limitations of urologic X-ray tables. In these instances, we have treated the patients in bed in the supine position. Obviously, proper execution of RIRS is more demanding because of patient positioning and since fluoroscopic guidance is not available. Regardless, it has been our experience that RIRS can be successfully performed. Intraoperative ultrasound is helpful in locating the stones and verifying the correct position of the indwelling stent at the conclusion of the procedure.

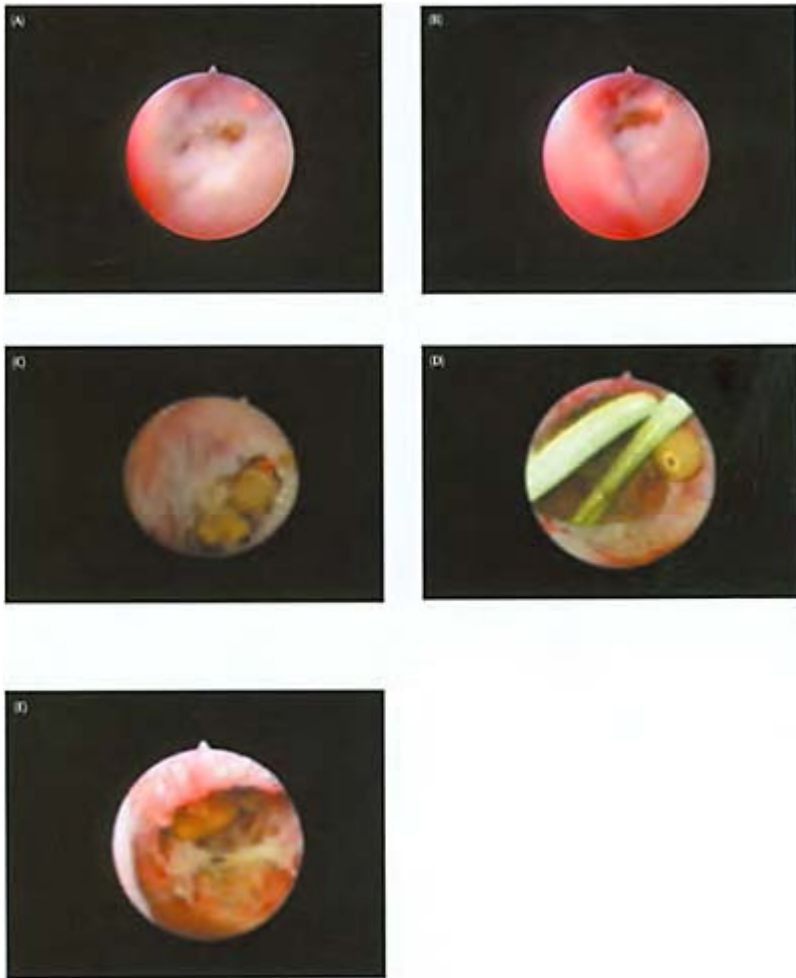


**Figure 30.12** Two-centimeter pelvic stone in patient with failure of liver transplant, end-stage liver disease and severe coagulopathy. RIRS with direct contact Holmium stone fragmentation can be safely performed. (A) IVP film shows the non-obstructing 2.0 cm stone in renal pelvis (stent seen is in

duodenum; migrated from common bile duct). (B and C): RIRS with semi-rigid 9.5F ureterscope; various stages of central stone vaporization are depicted (holmium 365  $\mu\text{m}$ , 20–10 W).



(D, E, F) After vaporization of the core, the 'shell' fragments and the gravel is removed with the rigid 4.5F grasper. (G, H) The dependent calyces are inspected with the flexible scope and small gravel removed.



**Figure 30.13** Retained mid renal stones s/p 2×SWL treatment (aviation pilot). (A) Stones are trapped behind stenotic intrarenal segment. Holmium laser incision is performed (7.5F instrument, 200 urn fiber, 10 W). (B and C) Further incision reveals the well fragmented stone gravel. (D) The

calyx has been completely incised, a wire is curled in the calyx to facilitate wash-out of the well fragmented gravel. The gravel is then retrieved from the kidney with a Nitinol basket. (E) The calyx is clean but for one piece which is removed with a zero-tip Nitinol basket. Note the fibrinous material s/p E-SWL (a common cause for retained stones in lower calyces).

Picture series: Upper pole diverticulum with stones and recurrent infection; s/p SWL times 3.

Picture series: 2.0 cm renal pelvic stone in patient with failure of liver transplant, end-stage liver disease and severe coagulopathy. RIRS with direct contact Holmium stone fragmentation can be safely performed.



**Figure 30.14** RIRS can be performed in the office setting under topical anesthesia to the urethra. Diagnostic inspection for surveillance of upper tract TCC and small stone residual are the common indications. No stenting is necessary.

*Retrograde intrarenal surgery for aviation pilots*

Aviation pilots need to be free of stones, which pose a potential risk of in-flight colic and incapacitation.<sup>48,60</sup> Over the years, a number of pilots have been referred to our center, usually with retained stones after several sessions with ESWL. Mostly, they had a prolonged period of inability to pursue their work. It is clear that endoscopic surgery is to be employed in these cases in order to assess the cause of previous failure and to effectively render the patient stone free. RIRS is the treatment of choice for the small-to-moderate stone burden, and PCNL is the choice for larger or more complex stone situations and also for failure of RIRS. As is shown in Figure 30.13, intrarenal stenosis can be the reason why well-fragmented stone gravel does not clear despite one or more sessions with ESWL. It is therefore our practice and recommendation to perform the appropriate endoscopic procedure as the firstline treatment in order to assure a speedy road to a stonefree state and return-to-flight eligibility status.

**Conclusion and future role of retrograde intrarenal surgery**

The technique of RIRS has clearly established itself as a valid treatment option for the appropriate patient with stone disease, intrarenal stricture, and upper tract transitional cell carcinoma. Continuous improvement of the technique and development of more versatile and durable instruments and accessories have resulted in a wide range of indications. RIRS enjoys high success rates with low morbidity and is an outpatient procedure for almost all patients. Accordingly, the indications for ESWL have been reduced and the threshold for performing PCNL has been pushed upward. Further improvements will include the more frequent use of RIRS with topical anesthesia only and special techniques to facilitate stone vaporization and clearance from the lower calyx location.

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# 31

## Endoscopic management of ureteral stones

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### Introduction

Ureteral calculi are often symptomatic and require treatment for the relief of symptoms or obstruction. Even those stones that can be expected to pass require attention to be certain that the stone passes and does not cause silent, symptom-free obstruction. When treatment is required, there are several options available. Endoscopy offers the highest success in most patients and should always be considered.

### Signs and symptoms

The symptoms of ureteral calculi are well known. The presentation is often acute and clinically very prominent. The patient usually experiences severe intermittent flank pain that frequently makes him writhe around in contrast to the patient with acute peritonitis.<sup>1</sup> The pain often radiates to the ipsilateral groin, testis, or labius majorum, especially when the calculus is lodged in the distal intramural ureter. Urgency and frequency can also develop when the calculi pass into the distal ureter. Nausea and vomiting are frequently associated with renal colic because celiac ganglia innervate both the kidneys and the stomach. Gastrointestinal disturbances such as ileus or diarrhea may also be present and may complicate the diagnosis. The patient usually has elevated heart rate and blood pressure secondary to pain. However fever is infrequent in the absence of infection.<sup>2</sup> The exception is complete obstruction with forniceal rupture and urinary extravasation.

### Diagnosis

Urinalysis may reveal microscopic or gross hematuria.<sup>2</sup> However, the sensitivity and specificity of urinalysis as an indicator of urolithiasis is 85.5% and 42.6%, respectively,<sup>3</sup> while the incidence of negative hematuria in patients with urolithiasis based on urinalysis alone is 14.5%.<sup>3</sup> Pyuria may be present even in the absence of infection, but is usually not severe. Occasionally upon light microscopy of the urine one can see crystals that may help identify stone composition.

Plain radiographs of kidneys, ureters, and bladder (KUB) will reveal 90% of renal and ureteral calculi. Calcium oxalate and phosphate stones are the most radiopaque and are easily visible on plain films except when obscured by overlying bone. Struvite (magnesium ammonium phosphate) and cystine calculi are not as radiodense and may be more difficult to see on a plain radiograph. Calculi composed of uric acid, xanthine,

matrix, triamterene, dihydroxyadenine and indinavir are radiolucent and will not be seen on plain radiographs.<sup>2</sup>

Intravenous pyelography is employed to indicate renal function and define drainage and collecting system anatomy. The intravenous urography (IVU) criteria for diagnosis of ureteral calculi are the presence of visible stone within the ureter, unilateral dilatation of an opacified ureter above a dense structure or a filling defect, and delay of appearance of contrast media into the renal collecting system as compared to the opposite side. Delayed films with the bladder empty improve diagnostic accuracy in defining the site of obstruction. Sourtzis et al found the sensitivity of IVU in detection of urinary calculi to be 66% as compared to a 100% sensitivity of unenhanced helical computed tomography (CT).<sup>4</sup>

The diagnostic accuracy of ultrasound (US) scanning and excretory urography was compared by Saita et al in 157 patients with ureteral stones. The overall accuracy was 78.3% for ultrasound and 81.5% for excretory urography.<sup>5</sup> These rates were 83.2% and 85% respectively, in the cases of upper ureteral calculi, and 68% and 74%, respectively, in the cases of lower ureteral stones. However, when the modalities were combined the diagnostic accuracy rates increased to 98%, 94%, and 96.8% for upper, lower, and all stones, respectively. In the study of Choyke the falsenegative rate of ultrasonography was between 9 and 13% with a negative predictive value of 76%.<sup>6</sup> It is difficult to identify calculi within the ureter on ultrasonography unless there is dilatation, which leads to a hyperechoic area and acoustic shadowing. In the upper third of the ureter the lower pole of the kidney serves as an acoustic window and helps detect the stone shadows. The full bladder serves the same role for the intramural ureter. However, calculi in the midureter are very difficult to detect.

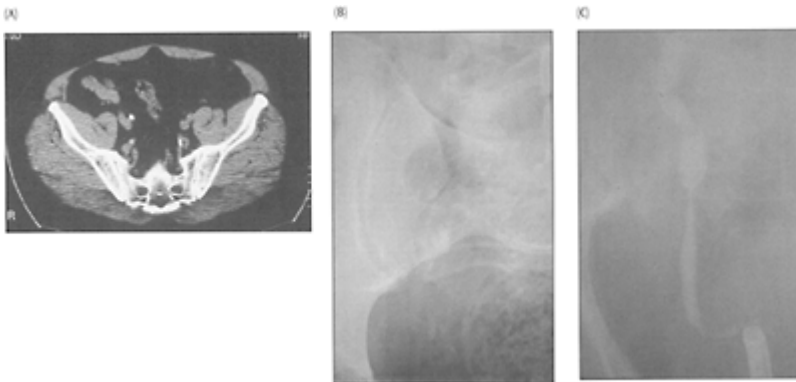
Unenhanced helical CT has emerged as the modality of choice when evaluating patients presenting with acute flank pain. The sensitivity of helical CT ranges from 96 to 100% and the specificity from 92 to 100%.<sup>4</sup> With the exception of indinavir stones, CT detects all types of calculi with great accuracy. On CT, stones have high attenuation, making identification easier. There are also useful indirect signs of an obstructing calculus, including perinephric stranding, hydronephrosis, and fluid in the perinephric and paranephric space seen following forniceal rupture.<sup>7</sup> When the calculus is present in the ureter, there may be a rim of soft tissue around the stone (the tissue rim sign), which helps differentiate a calculus from other calcification.<sup>7</sup> Another advantage of helical CT is rapid data acquisition. It is possible to obtain all the images in less than 1 min, the time it takes to hold one breath<sup>8</sup> (Figures 31.1–31.3).

Magnetic resonance imaging (MRI) is poor in evaluating patients with stones. However, the future role of MR urography may be imaging of children and pregnant women to minimize exposure to ionizing radiation. Also it



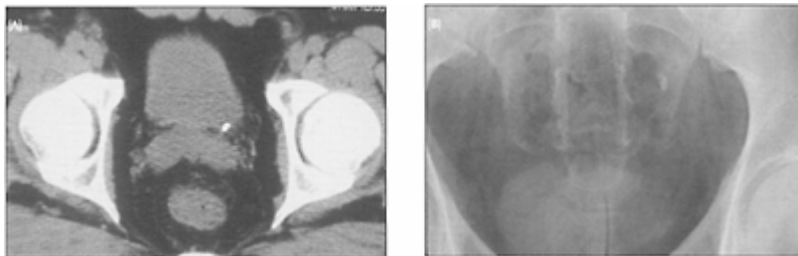
**Figure 31.1** A 4 mm proximal ureteral calculus is seen on a noncontrast CT scan. Although it was composed of calcium oxalate, it could not be seen well on an abdominal (KUB) radiogram. The patient was symptomatic and the stone was treated with flexible ureteroscopy and laser lithotripsy.

could be used in showing the anatomic details of the pelvicalyceal systems and ureters and in functional evaluation of kidneys, especially in patients in renal failure or contrast allergy.<sup>9-11</sup>



**Figure 31.2** (A) A noncontrast CT scan in a 58-year-old male with abdominal and flank pain demonstrates a calculus in the right midureter. A vascular calcification is seen in the left.

(B) A calcification is evident over the lower margin of the bony pelvis. (C) A retrograde pyelogram confirms the location of the calculus in the ureter. The stone was treated with flexible ureteroscopic holmium laser lithotripsy.



**Figure 313** Left flank and lower quadrant pain prompted evaluation with a CT scan, which showed the left mid-distal ureteral density (A). A KUB radiograph (B) demonstrates a 4×8 mm calcification in the same location. The patient had been anticoagulated for peripheral thrombophlebitis and pulmonary emboli. The stone was treated with rigid ureteroscopic holmium laser lithotripsy.

#### *Endoscopic diagnosis*

In a few patients the diagnosis of calculi cannot be made. In these same patients, who have symptoms and signs such as hematuria, strongly indicating ureteral calculus, but without radiologic confirmation, ureteral endoscopy can be a final arbiter to define the presence or absence of a calculus.

## Treatment options

### *Observation*

Most ureteral calculi will pass spontaneously.<sup>12</sup> The major factors affecting the probability of stone passage are the size of the stone, its location in the ureter, and any history of passing prior stones. Stones in the proximal ureter are less likely to pass than those in the distal part and the smaller calculi are more likely to pass spontaneously.<sup>13</sup> Irving et al did not find any calculi greater than 7 mm that passed without surgical intervention.<sup>14</sup> Segura et al in the American Urological Association (AUA) clinical guidelines summary reported that stones of < 5 mm in the proximal ureter pass spontaneously in 29–98% of patients, whereas stones of 5–10 mm in diameter pass in 10–53% of patients. In the distal ureter, stones less than 5 mm pass spontaneously in 71–98% of patients and stones of 5–10 mm pass in 25–53% of patients.<sup>12</sup> Miller and Kane developed a multiple linear regression model for prediction of days to stone passage:<sup>15</sup>

Days to stone passage =  $20.21 + 5.01 \times \text{size} - 4.23 \times \text{position} - 7.25 \times \text{side}$  (Size is 1, 2, 3 or 4 mm (for 4–6 mm stones)

(Position is equal to 1 for proximal, 2 for midureteral, and 3 for distal calculi)

(Side is 1 for left or 2 for right)

In their analysis 95% of 2–4 mm ureteral calculi pass spontaneously, but the passage may take as long as 40 days.<sup>15</sup> Overall, the time to stone passage is highly variable, and difficulty in controlling pain, persistent complete obstruction, infection, and other factors may mandate prompt intervention. Symptoms are not a reliable indication of obstruction, and one should follow the renal function with serial imaging during conservative treatment. The most sensitive technique to monitor renal function is isotope renography.<sup>13</sup> Serial sonography with renal Doppler calculated resistive indices is readily available and accessible. Whitfield summarized indications for abandonment of conservative management: evidence of infection above the site of obstruction; intractable pain for >72 hours; stasis of stone; evidence of persistent renal impairment; and certain socioeconomic circumstances.<sup>16</sup>

### *Medical therapy*

Medical treatment of ureteral calculi has not found widespread application because of the development of very effective interventional therapies, the high rate of spontaneous stone passage, and poor efficacy.<sup>13</sup> However, uric acid stones reflect one exception in that they can be dissolved if the pH of urine is raised to 6.5–7. The urine can be alkalinized by potassium citrate and sodium bicarbonate therapy. Stone dissolution may take several weeks and may not be applicable in a patient with severe and acute symptoms or complete obstruction. Frequent pH levels should be obtained to be certain of adequate alkalinization and to adjust the medication appropriately.<sup>13</sup>

Ketorolac is an effective medication to treat renal colic.<sup>17</sup> It acts centrally at the brain to decrease the sensation of pain and at the renal medulla, where it blocks the synthesis of

prostaglandin E<sub>2</sub>, thus decreasing glomerular filtration rate (GFR) and subsequent urine output.<sup>17</sup> Ketorolac also decreases ureteral spasm and ureteral edema by blocking prostaglandin E<sub>2</sub> production at the point of impaction.<sup>19</sup> Larkin et al compared intramuscular ketorolac with meperidine for treatment of renal colic in a prospective, controlled, double-blind randomized trial. A significantly greater improvement in the visual analogue scale pain scores was seen with ketorolac at 40, 60 and 90 min. Also, the time to discharge was 52 min earlier in the ketorolac group.<sup>19</sup>

Ureteral muscle spasm and submucosal edema may contribute to calculi retention.<sup>17</sup> Cooper et al assessed if commonly used drugs could improve the clinical course of patients with symptomatic ureteral calculi. In a randomized fashion, treatment with acetaminophen, ketorolac, oxycodone and prochlorperazine (control arm) was compared to treatment with the same medications plus nifedipine XL, prednisone, and trimethoprim-sulfa (treatment arm). The treatment arm had higher stone passage rates (86% vs 56%), and fewer lost work days, emergency room (ER) visits, and surgical interventions.<sup>17</sup> The medications increasing stone passage included nifedipine, which was thought to decrease ureteral muscular spasm; prednisone, to decrease ureteral inflammation; and trimethoprim-sulfa, to reduce urinary tract infections.

Proglia et al, in a randomized controlled trial, showed an increase in stone expulsion in patients with distal ureteral calculi treated with 30 mg of slow-release nifedipine and 30 mg of deflazacort. A statistically significant difference was observed in both the expulsion rate (79% vs 35%) and expulsion time (7 days vs 20 days).<sup>20</sup> The patients in the treatment group used less diclofenac for pain control and the difference was statistically significant. Therefore, medical therapy may be an effective adjunct in the treatment of ureteral stones.

### *Extracorporeal shock wave lithotripsy*

If ureteral calculi fail to pass spontaneously, the leastinvasive intervention is extracorporeal shock wave lithotripsy (ESWL), which may not be the most successful.<sup>16</sup> The success rate for ESWL depends on many factors such as stone size, fragility, chemical composition, impaction, duration of obstruction, and radio density.<sup>21</sup> Hard stones such as calcium oxalate monohydrate may not break well with ESWL when compared to calcium oxalate dihydrate calculi when they are matched in size and location.<sup>13</sup> Success of ESWL also depends on stone location. The stone-free rate for proximal ureteral calculi treated with ESWL ranges from 57 to 96%, with 5–60% of patients requiring retreatment or an adjuvant procedure.<sup>12,22</sup> For midureteral calculi, the stone-free rates range from 60 to 85%, yet retreatment rates may be as high as 30%.<sup>23</sup> Distal ureteral calculi stone-free rates range from 84 to 96% and retreatment rates range from 8 to 51%.<sup>22</sup> Large stones in the upper ureter, just above the common iliac vessels or at the uteropelvic junction (UPJ), which have been lodged for over 1 month, will be associated with ureteral edema, which may hinder adequate fragmentation by ESWL.<sup>13</sup> Overall, ESWL is more effective for smaller stones.<sup>22</sup> For large stones, ureteroscopy is clearly more successful. ESWL and ureteroscopy are both efficacious for distal ureteral calculi, but ureteroscopy has higher stone-free rates, with a success rate close to 100%, and carries minimal morbidity.<sup>12</sup> For ESWL, we presently elect ureteral calculi, that are small (<1 cm), fragile-appearing, non-impacted, and radiopaque.



*Percutaneous nephrostomy and antegrade ureteroscopy lithotripsy*

Percutaneous nephrostomy (PCN) drainage is useful in the treatment of silent infections and obstructing ureteral calculi. PCN has the advantages over retrograde ureteral stent placement for drainage. PCN also provides a means of monitoring urine output. The proponents of stent placement in the setting of an obstructed infected system cite greater patient comfort and decreased morbidity with an internalized stent. There is no statistically significant difference between the two modalities.<sup>24</sup> The choice of drainage can be individualized according to presenting signs, with open drainage employed as a primary or secondary modality. Antegrade ureteroscopy can be employed after percutaneous decompression, often with minimal anesthesia.

*Percutaneous endoscopy*

A percutaneous nephrostomy offers another site for endoscopic access to the ureter. It can be the preferable choice if a nephrostomy has been placed previously for drainage when the dilated ureter is inaccessible. Rigid and flexible ureteroscopes and nephroscopes can be used with any available endoscopic lithotripter.

*Laparoscopic and open ureterolithotomy*

In the era of very successful endoscopic and SWL treatments for ureteral calculi, open ureterolithotomy should be a very rare procedure. Some of the possible indications include failure of endoscopic lithotripsy, complications of ureteroscopy not amenable to endoscopic therapy, calculi associated with ureteral stenosis, and malformations requiring simultaneous open surgery for other indications.<sup>13,25</sup>

With advancement of laparoscopic techniques, the role of open ureteral surgery has diminished even further. The indications for laparoscopic ureterolithotomy include calculi that cannot be accessed ureteroscopically or cannot be fragmented and those associated with ureteral strictures requiring ureteral repair.<sup>26</sup> Its advantages include high probability of removing the calculus in one procedure without leaving residual fragments. Reported complications, however, are injury to adjacent structures, including iliac vessels and colon, and urine leak with formation of postoperative urinoma. Laparoscopy may be employed in patients who failed other treatments and have large impacted calculi.

*Ureteroscopy*

Advances in ureteroscopic instrumentation have brought ureteroscopy to the forefront of treatment of ureteral calculi. The addition of small-diameter rigid and flexible ureteroscopes has enabled urologists to treat not only ureteral calculi but also stones in the intrarenal collecting system. The addition of the holmium laser for endoscopic lithotripsy has further improved the success rate and expanded the indications for transurethral stone therapy.<sup>27</sup> Tawfik and Bagley reported 98.7% success rate with ureteroscopic treatment in 82 cases of ureteral calculi (29 proximal, 19 mid, and 34 distal). Only one patient with a proximal ureteral calculus required retreatment for a 4 mm residual fragment in the kidney. Thus, with a single case of retreatment a 100% success rate was achieved.<sup>28</sup> Fabrizio et al achieved 89% success rate and 77% stonefree

rate in the ureteroscopic treatment of intrarenal calculi<sup>29</sup> and Grasso et al reported 91% overall success rate with ureteroscopic treatment of lower pole calculi,<sup>30</sup> which is by location technically more demanding than ureteral calculi.

The success rate for stones in the proximal ureter is dependent on multiple factors including the availability of flexible endoscopes. Stones may be difficult to reach in muscular men with prominent psoas muscles, but should be amenable to the flexible ureterorenoscopy even if the calculus migrates cephalad into the kidney during manipulation.<sup>12</sup> Success is dependent in part on the experience of a surgeon, and the availability of advanced instrumentation.

Distal ureteral calculi can be treated with a very high success rate using semirigid fiberoptic ureteroscopes. Bagley et al compared success rates in multiple series of ureteroscopy and ESWL for treatment of distal ureteral calculi. In their review an average stone-free rate with distal ureteroscopy was 94.9% (range 94–100%) vs 87.2% for ESWL.<sup>13</sup> Furthermore, when the success rate for ureteroscopy was analyzed separately for series reported before and after 1996 the average success rate rose by 5% (91.2% vs 96.4%), thus suggesting that advancement in technology increases the treatment success. Ureteroscopy today is usually performed as an outpatient procedure in most patients and represents a safe and effective method of treatment for the majority of ureteral calculi.

Relative contraindications to ureteroscopy include patients with evidence of active urinary tract infection and not on appropriate antimicrobial therapy. Ureteroscopy should be delayed until the infection is treated with appropriate antimicrobials. During ureteroscopy with irrigation, pyelotubular, lymphatic, and venous backflow can occur and can lead to intravascular dissemination and sepsis.<sup>31</sup> Patients with obstructing calculi, infection, and impending sepsis should be drained with either percutaneous nephrostomy or passing of a ureteral stent prior to defini-

tive endoscopic lithotripsy. A very large prostate, especially with a prominent median lobe and J-hooking of the distal ureters, may prevent rigid ureteroscopy. Attempts to pass the rigid instrument proximally out of the pelvis may bend the instrument and with rod lens endoscopes a crescent-shaped field of view may appear.<sup>31</sup> This emphasizes the importance of the flexible endoscopes, which can traverse these segments.

Passage of the ureteroscopes may be difficult in those with a history of ureteroneocystostomy, especially via a cross-trigonal (Cohen) reimplantation and with a history of complex ureteral strictures. In the case of reimplantation, access may be achieved by passing a guide wire from a PCN antegrade into the bladder. Ureteral stricture may be dilated and stented prior to ureteroscopy.

### **Preoperative preparation**

Patients undergoing ureteroscopy require general or spinal anesthesia, with reports of successful ureteroscopy under local anesthesia with sedation.<sup>13</sup> Standard preoperative preparation with assessment of renal function, hemoglobin, white blood cell count, and chest radiograph is performed. Patients with hypertension, diabetes, and other risk factors for coronary artery disease require a preoperative electrocardiogram (ECG) and may need a full cardiac evaluation, especially for those with high risk. Preoperative antibiotics are routinely given prior to induction of anesthesia; a first-generation cephalosporin or fluoroquinolone will adequately cover common urinary pathogens.



## Equipment

Distal ureteroscopy is most frequently performed with semirigid endoscopes (Table 31.1). These instruments incorporate one, two, or three working channels within the smaller outer diameter of the endoscope. Instruments used through the endoscope allow for both stabilization of calculus and simultaneous laser fragmentation.<sup>31,32</sup> Tip diameter is frequently less than 7F to facilitate placement of the instrument into the ureter without prior dilatation. The semirigid endoscopes vary in length up to 43 cm and can reach the renal pelvis. It is not, however, considered an appropriate instrument for passively deflected intrarenal procedures.<sup>33</sup> With fiberoptic imaging bundle, these ureteroscopes can be slightly bent without losing any portion of the visual field.

Actively, deflectable, flexible ureteroscopes are complementary and are employed in the proximal ureter and intrarenal collecting system. These endoscopes range in size, with an average 8.5F shaft, and a 7.5F or less tip diameter. The actively deflectable segment can be deflected by a thumb lever located on the handle. The tip deflection ranges from 170° to 270° up and down in the newest versions.<sup>32</sup> The passive secondary deflecting segment is used to access the lower pole and is based on an inherent weakness in the stiffness of the shaft that is located just proximal to the actively deflecting segment (Figure 31.4) By advancing the instrument against the upper margin of the renal pelvis, the endoscope shaft will buckle into the lower pole.<sup>31</sup> The newer flexible ureteroscope utilizes an 'active' secondary deflecting segment, which allows for easier access into the lower pole and accessory placement.

Most flexible ureteroscopes have a 3.6F working/irrigating channel. The channel is essential for passing instruments and simultaneously irrigating to maintain visibility within the urinary tract. The working channel is soft and Teflon-based. During deflection, its shape changes from circular to oval and thus can prevent passage of certain accessories.<sup>31</sup> Thus, when the ureteroscope is deflected it is more difficult to pass instruments through the working channel. Accessories must be <3F and should be passed through a flexible ureteroscope while in a straight position.

**Table 31.1** *Ureteroscopic treatment of calculi: effect of instrument*

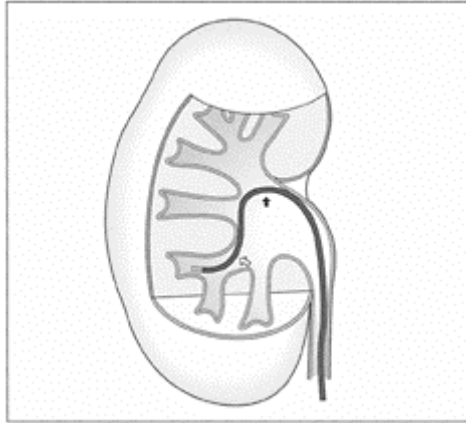
|   |   | Year  |                              |                        |  |
|---|---|---|------------------------------|------------------------|--|
|   |  |  | 1996                         | 1999                   | 1999–2002                                |
| Endoscopes                              | Rigid   | 10F flexible  | 7F rigid 7.5F flexible       | 7F rigid 7.5F flexible | 7.5 flexible                             |
| Lithotriptors                           | US, 5F EHL  | 3F EHL  | 1.6–1.9F EHL                 |                        |  |
|   |   | 60 mJ pulsed dye laser  | 140 $\mu$ J pulsed dye laser | Holmium laser          | Holmium laser                            |
| Instruments                             |   |   |                              |                        | 2.6F nitinol grasper 3.2F nitinol basket |
| <i>Stones removed ureteroscopically</i> |   |   |                              |                        |  |
| Ureteral                                |   |   |                              |                        |  |
| Proximal                                | 50  | 95  | 96                           | 98                     |  |

|        |    |    |    |       |
|--------|----|----|----|-------|
| Mid    | 62 | 69 | 91 | 99    |
| Distal | 95 | 61 | 93 | 98    |
| Renal  |    | 96 |    | 76–91 |

Lower pole

77–91

EHL, electrohydraulic lithotripsy; US, ultrasound.



**Figure 31.4** Active (top arrow) and passive (lower arrow) flexible ureteroscopic deflection. Lower pole caliceal ureteroscopic access is obtained via both active and passive secondary deflection. (Reproduced with permission from Smith's textbook of endourology, Volume 1, page 448, figure 32–4. Published in 1996 by Quality Medical Publishing, Inc., St Louis.)

Many working instruments are now available in sizes less than 3F, but the 2.5F instruments are especially useful since they leave adequate room for the irrigating fluid. Instruments used with the flexible ureteroscope include wire-pronged graspers, baskets, snares, laser fibers, fulgurating electrodes, and electrohydraulic lithotripsy (EHL) probes.<sup>33</sup> Effective, flexible, and reversible grasping devices are essential for successful ureteroscopic stone treatment.<sup>34</sup> A common accessory used to extract ureteral calculi is a 2.5F Teflon-sheathed, wire-pronged (three-prong) grasper.<sup>31</sup> It causes minimal loss of deflection and easily releases stones or fragments that are too large to extract, thus minimizing the risk of instrument entrapment with the calculus.<sup>35,36</sup>

There are multiple baskets designed for removal of calculi or their fragments. One of the earliest is the helical or Dormia basket, which was designed for stone retrieval within

the ureter. Even impacted calculi can be engaged in this basket by 'rotating' the round wires around the stone. Tipless basket designs are made of nitinol, an alloy of nickel and titanium. Nitinol wires do not kink and are also very flexible. The nitinol baskets are available in sizes as small as 2F and are effective in engaging stones because the basket tends to return to its original shape.<sup>33</sup> Also, the Teflon sheath of nitinol baskets is very flexible, allowing a near full range of deflection of the flexible endoscope, especially with the 2.4F basket.<sup>37,38</sup>

Endoscopic lithotrites have to utilize flexible small diameter probes to be used via a flexible ureteroscope. Ultrasonic lithotripsy used extensively in the 1980s through rigid ureteroscopes has been replaced by other modalities. Ultrasound probes lose power when deflected and cannot be used effectively in the flexible and semirigid ureteroscopes.<sup>32</sup>

EHL is based on the effect of an electric discharge in a liquid medium that generates a hydraulic shock wave, which then impacts on the stone. The discharge is unfocused and can produce some shock wave damage to surrounding tissue. The early experience with EHL was plagued by ureteral perforations and strictures, but was associated with large >5F probes. When used with 3F or smaller probes under direct vision and endoscopic control, EHL was shown to be safe and effective.<sup>39,40</sup> Yet, EHL does not fragment hard stones and may cause ureteral wall trauma if the probe is discharged too close to the ureteral wall.

Ballistic lithotriptors use electromagnetic energy (EKL) or air pressure (Swiss LithoClast)) to fragment stones. EKL propels a rigid metal probe through a hollow cylinder to fragment the stone.<sup>41,42</sup> Swiss LithoClast uses compressed air, which propels a small projectile against the probe, causing the probe to oscillate at a frequency of 12 cycles/s. The two devices are equally effective in terms of stone disintegration.<sup>42</sup> Ballistic lithotriptors were shown to have a good margin of safety in vitro<sup>43</sup> and clinical studies.<sup>41</sup> However, the devices often do not yield fragments less than 4 mm, especially with fragmenting hard stones in a dilated ureter.<sup>41</sup> Furthermore, EKL probes cannot be placed through a flexible endoscope and, thus, are unable to treat proximal ureteral calculi. Retrograde stone migration is another limitation, especially in dilated systems.

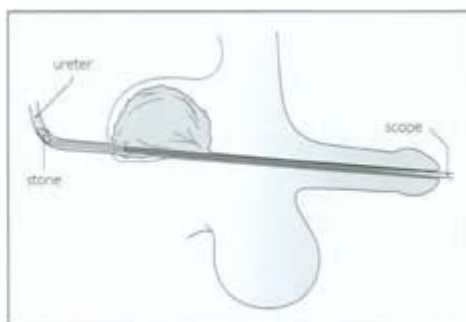
Lasers use pulsatile light delivered through small, flexible quartz fibers to a stone surface. The power is concentrated within an area on the stone surface equivalent to the surface area of the laser fiber. Since the laser fibers are of small caliber, the power density is very high.

The pulsed-dye thermal-free (coumarin is the lasing dye) laser fragments stones with a pulse duration of 1 ms and a wavelength of 504 nm (green light). A shock wave is produced because the high power density, when absorbed by the stone, is sufficient to remove free calcium ions and electrons off the stone surface.<sup>31</sup> Fragmentation occurs when laser pulses are delivered with the fiber touching or closely adjacent to the stone.<sup>31</sup> The deliverable energy is limited by the diameter of the fiber. Energies up to 90 mJ can be transmitted through a 200 µm fiber and up to 140 mJ through a 320 µm fiber. However, harder calculi such as calcium oxalate monohydrate stones require higher energies for fragmentation and consequently larger fibers must be used. The larger fibers significantly limit active deflection of the ureteroscope and compromise access to the stone.<sup>32</sup> Pulsed-dye lasers rarely produce stone fragments less than 4 mm and may require fragment extraction.<sup>44</sup>

The holmium:yttrium-aluminum-garnet (Ho:YAG) laser produces a 2150 nm wavelength of light energy. The energy is delivered in pulsatile manner through a low water density quartz fiber.<sup>32</sup> The holmium:YAG laser is a thermal device which superheats water, creating vaporization bubbles at the tip.<sup>45</sup> The vaporization bubbles do not produce a shock wave, but rather destabilize stones, fragmenting them into small fragments and fine dust. The fiber diameter does not restrict the amount of deliverable energy. Even a 200  $\mu\text{m}$  fiber delivers enough energy to fragment stones of any composition. However, the size of the vaporization bubble is directly proportional to fiber size and, therefore, large calculi will be fragmented more efficiently with larger laser fibers. The holmium:YAG laser has been shown to have a wide margin of safety. The high temperature generated at the tip drops off significantly even at a few millimeters away from the fiber when used in saline irrigation and therefore does not inflict thermal damage to surrounding tissues.<sup>45</sup> A number of investigators have reported a very high success rate (92.6–100%) with holmium laser ureterolithotripsy without any evidence of postoperative ureteral stricture disease (Table 31.2).<sup>28,46,47</sup>

### Technique

Distal ureteroscopy can be performed with a semirigid ureteroscope. One technique is to pass a Teflon-coated guide wire into the ureter, advancing it beyond the calculus and into the proximal collecting system. If the stone is large, especially  $>2$  cm, it may be difficult to pass a standard guide wire and thus a hydromer-coated wire with an angled tip may be needed to bypass the stone. If it is impossible to pass the guide wire, the ureteroscope may also be used to place the safety wire under direct vision beyond the calculi. Once the wire is passed, it is fixed in place to serve as a safety wire. The ureteroscope is then introduced into the ureteral orifice adjacent to the safety guide wire (Figure 31.5). When placement of the ureteroscope is difficult, another wire may be placed through the



**Figure 31.5** The rigid ureteroscope is introduced under direct vision adjacent to the safety guide wire. (Reproduced with permission from Campbells urology, 8th edn, Volume 4, page

2863, figure 80–19a. Published in  
2002 by WB Saunders, Philadelphia.)

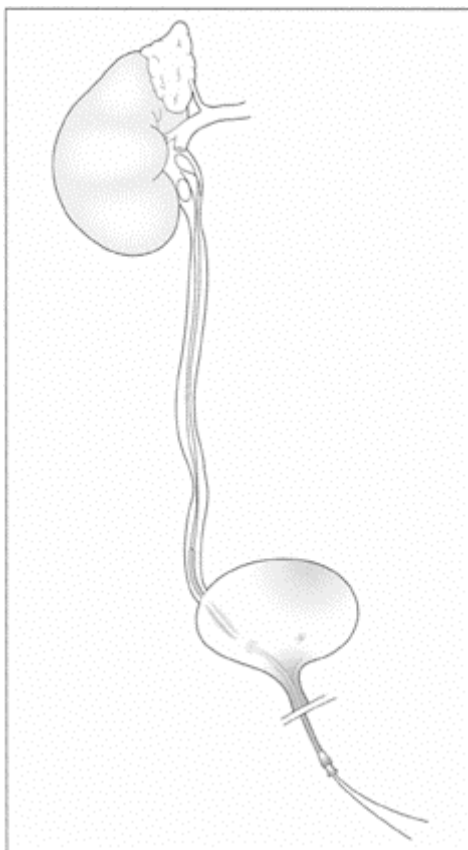
working channel to be used to open the ureter. The ureteroscope is then advanced between the two wires under direct vision. If that maneuver is unsuccessful as well, the ureteral orifice can be dilated with a dual-lumen catheter or a balloon dilator (~8F). The ureteral lumen must always be kept in view along with the safety wire. This is achieved by rotating the ureteroscope while advancing or by placing a second guide wire to straighten the ureteral segment, or by using pressurized irrigation to distend the ureteral walls.

Flexible ureteroscopy also begins by placing an initial guide wire. A second working wire can be passed using a double-lumen catheter or tapered 8/1 OF Amplatz dilator (Figure 31.6) The endoscope is then advanced under fluoroscopic guidance over this guide wire into the orifice to the level of the calculus to be treated. It is important to maintain a straight guide wire and prevent kinking. The working channel is located somewhat eccentrically at the

**Table 31.2** *Comparison of endoscopic lithotriptors*

| Lithotripter | Effective fragmentation | Safety | Stone removal | Cost |
|--------------|-------------------------|--------|---------------|------|
| EHL          | +++                     | +      | 0             | +    |
| US           | ++                      | +++    | ++++          | +    |
| Impact       | ++++                    | +++    | 0             | +    |
| Lasers       |                         |        |               |      |
| Pulsed-dye   | ++                      | +++    | 0             | ++++ |
| Holmium      | ++++                    | ++     | ++            | +++  |

EHL, electrohydraulic lithotripsy; US, ultrasound.



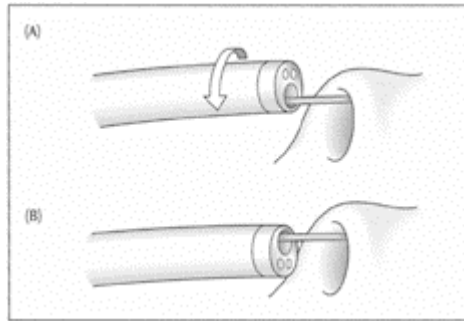
**Figure 31.6** After initial guide wire introduction, a secondary guide wire is introduced via a tapered 8/1 OF Amplatz dilator. (Reproduced with permission from Marshall, textbook of operative urology, page 41, figure 6–2. Published in 1996 by WB Saunders, Philadelphia.)

tip of ureteroscope and therefore the ureteroscope may require rotation so that the narrower portion of the tip approaches the overhanging lip of the orifice (Figure 31.7A and B). Thus, the guide wire lifts the orifice and allows the wider portion of the tip to pass through the intramural tunnel.<sup>36</sup>

Irrigation with normal saline must be maintained during ureteroscopy and stone fragmentation. It clears the visual field of small stone fragments and debris. During active



laser fragmentation, multiple tiny stone fragments and dust are released, obscuring the view. Pressurized irrigation may be needed to clear the visual field in this setting



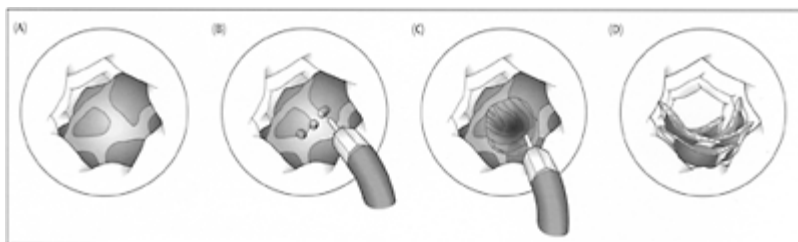
**Figure 31.7** (A) The working channel on the flexible ureterscope is eccentrically located, which impedes passage into the ureteral orifice. (B) The ureterscope will often need to be rotated until the guide wire is located at 12 o'clock. Thus, the ureterscope can be introduced in the ureteral orifice unencumbered. (Reproduced with permission from Campbell's urology, 8th edn, Volume 4, page 3312, figure 97–2A and B. Published in 2002 by WB Saunders, Philadelphia.)

(i.e. power irrigation). It can be achieved using a manually powered syringe or a pressurized bag. During lengthy endoscopic lithotripsy, the bladder must be drained intermittently with either a catheter or a working sheath.

#### *Laser lithotripsy technique*

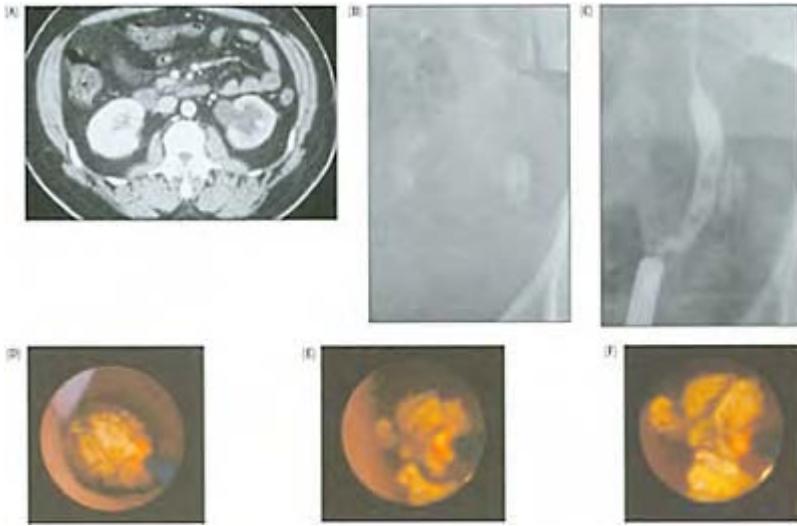
The aim of laser fragmentation is to convert the volume of stone material to dust. The energy per pulse and the frequency of laser pulses are dependent on the configuration of the ureteral segment containing the calculus and stone composition. In a dilated ureter, higher energies and frequencies will fragment promptly but may cause stone migration. Softer stones such as calcium oxalate dihydrate fragment well with lower energies. Calcium oxalate monohydrate calculi, which are particularly hard, require up to 1.0 J per pulse to achieve an ablative effect. The fiber tip must be held on the surface of the stone, sculpting it to smaller fragments. The fragmentation technique can be varied to change the size of the fragments. A cavity is first created in the surface of the stone (Figure

31.8A-D). The laser fiber is then applied slightly away from the edge to widen the cavity. The size of the fragments is achieved by adjusting the fiber closer or farther from the edge. The size of the fragments depends on the size of the ureteral lumen so that they can pass spontaneously. If these fragments are too large, then the laser energy can be employed to reduce the engaged fragments to a more easily extractable size. (Figure 31.9).



**Figure 31.8** (A) Impacted upper ureteral stone. (B) Small defects are created in the surface of the stone with a holmium laser. (C) Central laser vaporization of the ureteral stone creates a large cavity. (D) Remaining stone fragments are extracted or ablated to passable fragments.

(Reproduced with permission from Smith's textbook of endourology, Volume 1, page 450, figure 32–6, b, d, e f. Published in 1996 by Quality Medical Publishing, Inc., St Louis.)



**Figure 31.9** A CT scan showed pelvic radiodensities and left hydronephrosis (A) in a 67-year-old male with left lower quadrant pain. (B) Radiodensities seen on a KUB radiograph were confirmed as phleboliths and a retrograde pyelogram demonstrates the lucent ureteral calculi (C). The stones were treated with rigid ureteroscopic holmium laser lithotripsy. The red helium-neon finder beam is seen endoscopically at the tip of the 365  $\mu\text{m}$  fiber (D). The calculus is broken into fragments (E), which can be retrieved or reduced further to a size (F) that can pass.

Distal ureteral calculi can be reduced to relatively large fragments, which can then be easily retrieved from the ureter by using a grasper or a basket simultaneously. The size of the fragments can be estimated using the 1 mm safety guide wire as a guide.<sup>35</sup> When the residual fragments are about 3–4 mm, an attempt can be made to remove the largest fragment with a grasper to see if it can pass down the ureter. With only one channel, flexible ureteroscopic lithotripsy relies more on ablation than on extraction.

A ureteral stent is commonly left in place after endoscopic treatment of ureteral calculi. This practice is based on the premise that the stent may reduce postoperative

renal colic and stricture formation. However, the indwelling stent may cause bladder spasms and thus significant patient discomfort. Recently, the value of stenting has been questioned by several investigators.<sup>48,49</sup> Hosking et al reported on 93 patients who were not stented after rigid ureteroscopy for distal ureteral stones. None of the patients required repeated instrumentation and 87% either required no analgesics or had symptoms that were controlled with oral analgesics only.<sup>49</sup> Hollenbeck et al did not place a stent in 51 patients after ureteroscopic treatment of not only distal ureteral calculi but also of proximal and intrarenal stones. None of the patients in the nonstented cohort required repeated instrumentation.<sup>48</sup> Furthermore, the nonstented patients had fewer complications and the absence of a ureteral stent after ureteroscopy did not influence whether a patient would have a complication. Their criteria for not leaving a ureteral stent included ureteroscopy time less than 90 min; no significant trauma at the site of the stone; and no significant edema, trauma, or bleeding of the ureter or kidney.<sup>48</sup> Overall, if stenting is necessary, its duration should be as short as possible and leaving a dangle string will allow the patient to remove the stent at home without a doctor's visit and the discomfort of cystoscopy.

### *Complex ureteroscopic therapy*

Some ureteral calculi, because of their size and location in the ureter, may represent a special therapeutic challenge. Large (>2 cm) ureteral calculi are uncommon but, when found, are usually impacted and commonly associated with urinary tract obstruction. These calculi can be treated safely and effectively with semirigid or flexible ureteroscopy and holmium:YAG lithotripsy. A success rate as high as 95% has been reported in the complete ureteroscopic fragmentation of large ureteral calculi in a single session and 100% after a second-stage lithotripsy<sup>50</sup> (Table 31.3, Figure 31.10).

The treatment is facilitated by using large laser fibers (365–550  $\mu\text{m}$ ), fragmenting the calculus to fine debris, and employing continuous irrigation with simultaneous placement of a small bladder catheter. Infrequently, after endoscopic treatment of ureteral calculi, a residual fragment is seen radiographically with normal-appearing mucosa on endoscopic examination, suggesting a submucosal or extraluminal location. Treatment of these calculi represents a therapeutic dilemma. Endoluminal sonography provides an accurate image of periureteral anatomy.<sup>51</sup> Submucosal fragments appear as a highly echogenic focus with acoustic shadowing, and the



**Figure 31.10** A 15×30 mm proximal ureteral calculus and small intrarenal stones were treated with ureteroscopic laser lithotripsy. On a KUB radiograph 3 weeks later, there were three distal ureter fragments each less than 2–3 mm and a 5 mm group of small fragments in the right lower pole.

**Table 31.3** *Success of ureteroscopic treatment of large (>cm) upper urinary tract calculi*

| Ureteroscopic lithotripsy | Overall initial success   | Second-stage lithotripsy | Third-stage lithotripsy |
|---------------------------|---|--------------------------|-------------------------|
| Ureteral calculi          | 95% (20/21)   | 100% (21/21)             |                         |
| Renal calculi             | 76% (34/45), Grasso et al <sup>50</sup> 77% (23/30), El-Anany et al <sup>57</sup> | 91% (40/45)              | 93% (42/45)             |

size of the stone and the exact depth from the ureteral lumen can be defined. The patient with a single or few submucosal calculi can be treated endoscopically. The fragments can be extracted using a wire grasper or the beak of a rigid ureteroscope.<sup>54</sup> Direct endoscopic visualization and endoluminal US are used to monitor stone removal. A ureteral stent is placed to allow drainage and to prevent postoperative obstruction and stricture formation. Treatment of patients with multiple submucosal fragments is problematic, since removal of all the fragments is very difficult and ureteral strictures tend to form.<sup>52</sup>

Management of impacted ureteral calculi also presents a challenge. Impacted calculi are then defined by failure to advance and by the inability to pass a guide wire or a ureteral catheter. They are usually associated with ureteral obstruction.<sup>53</sup> ESWL is relatively ineffective for these stones.<sup>54</sup> The treatment is further complicated by the presence of reactive ureteral edema and inflammation and often underlying stricture. The endoscopic treatment of impacted calculi has been revolutionized with the advent of

small-caliber ureteroscopes and holmium laser lithotripsy. Now approaching and accessing the impacted calculus is less difficult and, even if a stricture is encountered, it can be incised with the holmium laser. A 96.2% success rate has been reported with an endoscopic treatment of impacted calculi in a single procedure and with minimal morbidity.<sup>55</sup>

Other difficult calculi to treat are those lodged at the ureterovesical junction, protruding through the ureteral orifice, and stones at the UPJ. The difficulty in treating UPJ stones lies in the possible migration of the calculus into the intrarenal location. The patient is positioned into a deep Trendelenburg position, with elevation of the ipsilateral flank so that the migrating calculus ends up in the upper pole calyx. Migration to the lower pole calyces can be especially problematic because of limitations of deflection, even by a 200  $\mu\text{m}$  fiber. Recently, a technique for displacing the calculus into a more accessible calyx with a nitinol basket or a grasper has been reported.<sup>37</sup> The stone is placed into a mid or upper pole calyx to prevent its migration during lithotripsy and to minimize the deflection of the endoscope. Kourambas et al<sup>37</sup> achieved a 90% stone-free rate using a 3.2F tipless nitinol basket or a 2.6F nitinol grasper to displace the calculus into a more favorable location prior to lithotripsy. Grasso and Ficazzola used a deep Trendelenburg position and a grasper to move the large fragments during lower pole ureteroscopic laser lithotripsy into a more cephalad position. They achieved an overall success of 91% and 94% for lower pole calculi of less than 1 cm.<sup>30</sup> When the in-situ treatment of lower pole calculi was compared to the displacement technique, a significantly higher success rate was observed with the displacement treatment.<sup>54</sup> For stones 1 cm or less treated in situ the success rate was 77% vs 98% success rate for those treated with displacement. For calculi greater than 1 cm, the difference was even more pronounced (29% vs 100% success rate).<sup>54</sup> The technique of stone displacement prior to lithotripsy may also be employed for treatment of ureteral calculi at the UPJ.

Distal ureteral calculi may be lodged at the orifice in a position that precludes easy access. There may be considerable edema, which may even obscure the orifice. The initial step again is to place a guide wire if possible. If the standard guide wire cannot be placed, then a hydrophilic wire, either straight or angle tipped, may be supported in a ureteral catheter and introduced into the orifice to pass the stone. If that is still not possible, then a direct approach with a rigid ureteroscope either to pass the wire or to fragment the stone can be used. As the stone is fragmented, an opening may appear between the stone and the ureteral wall. At that point, a guide wire is placed under direct vision to secure access to the ureter, and fragmentation of the stone is then completed. In rare instances, it is not possible to gain any access to the ureter or even to find the orifice. It then may be necessary to place a nephrostomy either to pass a wire into the ureter and into the bladder or to drain the kidney proximally. The vast majority of distal ureteral calculi can be treated ureteroscopically. Other techniques such as ureteral meatotomy or percutaneous approach should be reserved for the otherwise impossible cases.

Ureteroscopy carries a 0–6% rate of major complications. Operative time, the need for extraction of stones from the kidney and surgeon's experience are predictive of intraoperative and immediate postoperative complications of ureteroscopy.<sup>56</sup>

### Conclusions

Endoscopic lithotripsy is a safe and effective method for the treatment of ureteral calculi. Ureteroscopy performed with appropriate endoscopes and the holmium laser is the most successful treatment for ureteral calculi. It can be used for nearly any ureteral stone and should be considered a first choice in most patients.

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## 32

# Minimally invasive treatment of bladder calculi

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Bladder stones account for only 5% of urinary calculi in the Western world<sup>1</sup> and usually affect adult men with bladder outlet obstruction. In contrast to renal stones, bladder stones are usually composed of uric acid or struvite. Bladder stones in the pediatric population are becoming more frequent as the number of patients undergoing bladder-related surgery (augmentation cystoplasty, exstrophy repair, creation of Mitrofanoff stoma, urinary diversion) increases.

### Incidence

Depending on the type of procedure performed, the incidence of bladder stone formation in children with reconstructed bladders ranges from 5 to 52% (Table 32.1). The incidence with urinary diversions ranges from 3%<sup>7,8</sup> in nonrefluxing colon conduits to as high as 20% in some ileal conduit series<sup>9</sup> and 43% in Kock pouches.<sup>10-13</sup>

### Risk factors

Risk factors for stone formation include mucus production, decrease in urinary citrate levels, chronic bacteruria (caused by urea-splitting organisms), foreign bodies, and dehydration.<sup>9</sup> Mucus production can act as a nidus for stone formation and harbor urea-splitting organisms while causing poor drainage and stasis. Persistent infection causing alkalinization of the urine combined with chronic hypercalciuria create a suitable environment for stone formation. Conduits and pouches, especially Kock pouches,<sup>10</sup> created with nonabsorbable staples and suture are notoriously associated with stones.

**Table 32.1** *Incidence of bladder calculi*

| Type of bladder              | Incidence | Follow-up | Author                     |
|------------------------------|-----------|-----------|----------------------------|
| Augmentation cystoplasty     | 52%       | 4 years   | Palmer 1993 <sup>2</sup>   |
|                              | 10%       | 6 years   | Kronner 1998 <sup>3</sup>  |
|                              | 16%       | 4.9 years | Mathoera 2000 <sup>4</sup> |
| Exstrophy-epispadias complex | 26%       | 6 years   | Surer 2003 <sup>5</sup>    |
| Children on CIC              | 7%        | 3 years   | Barroso 2000 <sup>6</sup>  |
| no augment.+urethral cath.   | 5%        |           |                            |
| no augment+Mitrof. cath.     | 11%       |           |                            |
| augment, and urethral cath.  | 8%        |           |                            |
| augment, and Mitrof. cath.   | 10%       |           |                            |

CIC=clean intermittent catheterization; augment.=augmentation cystoplasty; Mitrof.=Mitrofanoff; cath.=catheter.

### Diagnosis

These stones are often found incidentally by plain film, pouchograms or loopograms, ultrasound, computed tomography (CT) scan, or endoscopy. Symptoms that suggest the presence of stones include gross hematuria, recurrent urinary infections, difficulty voiding or catheterizing, increased frequency of catheterization, lower abdominal fullness or discomfort, and incontinence.<sup>14</sup>

### Prevention

There are many strategies for prevention of bladder pouch stones. As with any stone, hydration is important in preventing stone formation. Frequent and complete catheterization/voiding can also help. In those with interposed bowel, daily irrigation of mucus from the bladder can minimize recurrent infection and stone formation. Many of these patients have low urinary citrate levels, raising the possibility that oral citrate repletion may help prevent these stones. Renacidin irrigation has been used to dissolve and prevent bladder stones composed of struvite or phosphate, whereas alkalinization for uric acid stones is also a viable option. Irrigation in a bladder that contains intestine is not

generally recommended, however, due to issues related to absorption. When prevention or conservative intervention is not successful, surgical options must be addressed.

### **Treatment modalities**

The historical treatment for bladder calculi is cystolithotomy. However, technological advances in endoscopic and lithotripsy equipment over the last two decades have made it possible for most bladder calculi in the adult population to be removed via the transurethral approach. Fragmentation can be accomplished with the use of mechanical means, electrohydraulic lithotripsy, ultrasonic lithotripsy, pneumatic lithotripsy (EHL), or holmium-YAG laser lithotripsy. However, the transurethral approach is not always possible in pediatric patients due to the smaller urethral caliber or the presence of a catheterizable stoma. In adult patients, as well, the risk of urethral injury and subsequent stricture is increased when lengthy transurethral procedures are performed for large or numerous calculi. In these patients percutaneous cystolithotomy is a suitable option.

#### *The technique of percutaneous cystolithotomy*

The technique of percutaneous cystolithotomy is straightforward and has evolved from previous experience with upper tract percutaneous procedures. A flexible or rigid endoscope is inserted into the bladder through an intact urethra. The pouch is filled with sterile saline and the previous site of a suprapubic tube is identified in those patients with prior bladder reconstruction. The site is transilluminated and examined visually to ensure there is no intervening tissue. Fluoroscopy is seldom required for percutaneous bladder access. A 16- or 18-gauge percutaneous access needle is inserted through the site under direct visualization from the endoscope. A guide wire is passed through the needle before the needle is removed. An 8/10 dilator set or 10F dual-lumen catheter can then be used to introduce a safety wire. This is followed by rigid coaxial dilation of the tract with an Amplatz set or a onestep trocar system under direct visualization. Following dilation, a 26 or 30F access sheath is placed and a nephroscope introduced through the sheath. Improved visualization facilitates fragmentation or intact removal of the stones without risk of urethral injury. Removal of all stones and fragments can be confirmed with a plain abdominal X-ray. A suprapubic catheter is inserted into the bladder through the access sheath, which is subsequently split and pulled back leaving the SP tube in place.

#### *Review of results*

Ikari et al reported an 89% success rate using ultrasonic fragmentation through a 26F nephroscope on the percutaneous treatment of bladder stones in 36 patients.<sup>15</sup> The 3 failures were due to inability to fragment the stone with the ultrasonic device. Twenty-two of these patients underwent concomitant TURP (transurethral resection of the prostate) or internal urethrotomy. Wollin et al reported a 100% stone-free rate when performing percutaneous suprapubic cystolithotripsy on 15 adult patients.<sup>16</sup> Patients were considered candidates for this approach if stone size >3 cm, multiple stones >1 cm were present, and patient anatomy precluded transurethral access. Using EHL, patients were

rendered stone free in one procedure (mean operative time 86 min) and no major complications occurred. Similar success was reported when utilizing this percutaneous approach with an ultrasonic lithotripter to treat stones of 1.2–3.1 cm in pediatric patients.<sup>17</sup>

Perhaps the greatest indication for percutaneous removal of bladder calculi is found in patients who have undergone urinary diversion. With improved oncologic therapies and procedures, it is now common for patients to live many years with reconstructed urinary systems created from bowel segments. In pediatrics as well, the continued refinement of reconstructive techniques has resulted in greater numbers of patients with augmented bladders and continent pouches. These patients are at greater risk for stone formation, yet standard endoscopic techniques can be limited by altered anatomy and increased risk of damage to surgically created continence mechanisms.

Multiple case reports appeared in the literature in the mid-1990s describing techniques for percutaneous treatment of continent pouch stones.<sup>18–20,21</sup> Franzoni et al presented their experience with percutaneous vesicolithotomy in 3 adult patients who had previously undergone continent urinary diversion, bladder neck closure, and appendicovesicostomy.<sup>20</sup> Using intact extraction and ultrasonic lithotripsy, all patients were rendered stone free and discharged the same day. More recently, Cain et al reported on a series of 13 pediatric patients who had developed stones following augmentation cystoplasty. Complete stone removal (intact or with laser or EHL fragmentation) was achieved in 92% without complication. One patient suffered a small bladder perforation and required conversion to open cystolithotomy.<sup>22</sup>

We reviewed our data of 11 pediatric patients undergoing 16 procedures with complete elimination of the entire stone burden in all patients, with one requiring a second-look procedure. The average operative time was 136 min and the average hospital stay was <1 day with 63% discharged the same day. Minor complications occurred in 5 of the 16 (31%) procedures and included ileus, hypothermia, and extravasation of fluid.<sup>23</sup>

Based upon the available literature, it appears that percutaneous approaches to bladder and urinary pouch calculi result in excellent stone-free outcomes. The few complications that have been reported were easily treated with conversion to traditional open cystolithotomy. Many of these patients have had significant prior reconstructive procedures on the urinary system and within the pelvis, which increases the complexity and the risk of complications when performing open cystolithotomy. With the relatively high rate of stone recurrence in augmented bladders and thus the need for repeated procedures, the importance of decreasing morbidity and hospital stay becomes evident.<sup>24</sup> Minimally invasive percutaneous procedures would therefore seem to be preferable to traditional open approaches. This, however, remains a controversial point.

### Stone recurrence

The data on stone recurrences in these patients are inconclusive, although some feel that intact extraction of stones reduces the stone recurrence rate compared with percutaneous or endoscopic approaches that rely on fragmentation<sup>14</sup> (Table 32.2). A series directly comparing open and

**Table 32.2** *Recurrence rate among stone formers*

| Type of bladder              | Recurrence rate | Treatment                   | Main author               |
|------------------------------|-----------------|-----------------------------|---------------------------|
| Augmentation cystoplasty     | 19%             |                             | Palmer 1993 <sup>2</sup>  |
|                              | 44%             |                             | Kronner 1998 <sup>3</sup> |
|                              | 54%             | Cystolitholapaxy            |                           |
|                              | 33%             | Open cystolithotomy         |                           |
| Exstrophy-epispadias complex | 38%             |                             | Surer 2003 <sup>5</sup>   |
| Children on CIC              | 32%             |                             | Barroso 2000 <sup>6</sup> |
|                              | 66%             | Endoscopically with EHL     |                           |
|                              | 33%             | Open cystolithotomy         |                           |
| Augmentation cystoplasty     | 66%             |                             | Docimo 1998 <sup>24</sup> |
|                              | 66%             | Open cystolithotomy         |                           |
|                              | 66%             | Percutaneous cystolithotomy |                           |

CIC=clean intermittent catheterization; EHL=electrohydraulic lithotripsy.

percutaneous techniques, however, found recurrence to be equally common in both groups,<sup>24</sup> suggesting that it is the underlying risk, and not technique, that accounts for high recurrence rates. The bladder stone recurrence rate in our most recent series was 58%, with a mean follow-up of 43 months.<sup>23</sup> Jarrett et al published a modification of the percutaneous approach to address recurrence.<sup>25</sup> They use an entrapment sac which is passed through the access sac. The calculi are then isolated from the remainder of the bladder or pouch inside this sac during fragmentation and removal. This eliminates the need to vigorously irrigate and remove tiny fragments at the end of the case.

## Conclusions

Although not the most frequently encountered, bladder stones and their management do merit discussion, especially when encountered in pediatric patients with reconstructed bladders. Many believe that open cystolithotomy remains the gold standard when addressing these stones with shorter operative times and decreased stone recurrence rates. However, because many of these patients have complex anatomy and have previously been operated on several times, and because they will probably need more bladder stone procedures in the future with high recurrence rates, thought should be given to a minimally invasive percutaneous procedure as described in this chapter.

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## 33

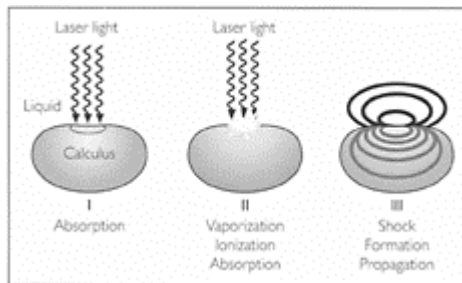
### Lasers in urology

Kenneth J Stallman and Joel MH Teichman

The use of lasers in urology has advanced dramatically over the past decade. In particular, the holmium:YAG laser (yttrium-aluminum-garnet) has become the primary laser familiar to urologists. The main areas that lasers are used in urology include intracorporeal lithotripsy and prostate applications (ablation or coagulation). In this chapter, we will focus primarily on those two urologic topics. We have divided the chapter into (1) laser lithotripsy and (2) urologic soft tissue laser applications. Within each section, we provide a review of relevant laser physics, followed by clinical urologic laser applications.

#### Laser lithotripsy

Pulsed dye, alexandrite, and Q-switched lasers have pulse durations between nanoseconds and up to 1.2  $\mu$ s. With such short pulse durations, these lasers deposit energy so quickly into water that the rapid energy accumulation



**Figure 33.1** Laser lithotripsy mechanism. When laser light deposits energy into liquid (I), rapid energy accumulates and causes stress confinement within the liquid. A cavitation bubble is developed (II). The cavitation bubble collapses symmetrically and synchronously. The



### collapse releases a high-intensity acoustic shock wave (III).

causes 'stress confinement' within water, creating a high-energy vapor bubble or cavitation bubble.<sup>1</sup> The spherical cavitation bubble expands and collapses upon itself. Because the spherical bubble collapses symmetrically and synchronously, the collapse releases a high-intensity acoustic pressure wave<sup>2,3</sup> (Figure 33.1). This pressure wave propagates circumferentially from the optical fiber tip. The stone fragments as a result of the pressure wave resulting from vapor bubble collapse. This method of fragmentation begins after the pulse duration has ended. The mechanism by which optical energy is converted into acoustic (pressure) transients is called photoacoustic lithotripsy.

In some short-pulsed lasers with high peak power (Q-switched lasers), a plasma is achieved. In this mechanism, the high peak power causes optical breakdown of the target stone, and the high-energy state is still associated with pressure transients. Thus, the mechanism is another form of photoacoustic lithotripsy. Alexandrite lasers tend to produce such fragmentation. A problem associated with these lasers is that the high peak power produced at the optical fiber tip produces fiber damage. Shards of optical fiber may be produced in the ureter.

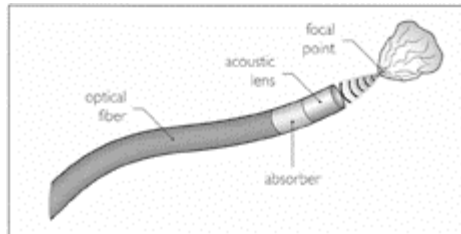
In photoacoustic lasers, peak pressure correlates with pulse energy and vapor bubble radius, and correlates inversely with optical fiber diameter. Thus, maximal lithotripsy effect may be achieved by using a photoacoustic laser at its highest pulse energy and smallest available optical fiber. (The high pulse energy and small optical fiber with the short pulse duration produce rapid accumulation of optical energy in water, producing a rapidly expanding spherical vapor bubble. The larger the sphere, the greater the energy is released upon its collapse.) Thus, there are competing physical factors when using photoacoustic lithotripsy laser devices. The most efficient lithotripsy (highest peak power) has the best chance of fragmentation but also the best chance of leaving shards of optical fiber in the ureter.

Photoacoustic lithotripsy (whether induced by plasma or vapor bubble collapse) produces irregular and unpredictable fragmentation. Stones are literally 'ripped' apart as a result of pressure effects. In the case of vapor bubble collapse, fragmentation is similar to electrohydraulic lithotripsy. With plasma, the fast plasma expansion produces internal pressure effects that are similar to microwaving popcorn. These lasers lack photothermal effects. Each of these lasers, by virtue of their short pulse durations, deposit energy quickly that is diffused without thermal accumulation or effect. The pulsed dye laser (coumarin green at a  $K=504$  nm) is well absorbed by red blood cells (and by most stone compositions). Thus, theoretically, any stray laser energy not directed on to stone, upon impacting soft tissue, would be absorbed efficiently by red blood cells and the energy dissipated and carried away without injury. Thus, these lasers have a high margin of safety.

In contrast to these short-pulsed duration lasers (pulse durations less than 10  $\mu$ s), the holmium:YAG laser has a long pulse duration of 250–350  $\mu$ s. Because of this long pulse duration, optical energy is deposited into water slowly relative to water absorption characteristics. As a result, the holmium:YAG vapor bubble is pear-shaped, so it collapses asymmetrically with weak cavitation effects, minimal plasma formation, and negligible acoustic pressure waves.<sup>1,4,5</sup> Holmium:YAG lithotripsy occurs through a

photothermal mechanism rather than a photoacoustic mechanism. Lithotripsy begins before the collapse of the vapor bubble.<sup>5</sup> In fact, holmium:YAG lithotripsy begins approximately 60  $\mu$ s into the pulse duration, while energy is still being deposited into the water and stone.

The photothermal mechanism requires direct absorption of optical energy by the stone. Optical energy must travel between the optical fiber tip and the target. In urologic endoscopy, optical energy travels through water, a medium which highly absorbs the holmium:YAG wavelength (2100 nm).<sup>6,7</sup> Because water attenuates holmium:YAG energy, some energy is 'wasted' in vaporizing a channel between the optical fiber tip and the target. Holmium:YAG transmission is enhanced through water vapor compared to liquid.<sup>7</sup> Thus, the initial portion of the holmium:YAG pulse vaporizes the water between the optical fiber tip and the stone surface and, through this vapor path, the beam transmits efficiently to the stone, a phenomenon called the 'Moses' effect (as though the laser were parting the water)<sup>8</sup> (Figure 33.2). The practical implication of the 'Moses' effect is that the optical fiber tip should be positioned as close to the target (stone or soft tissue) as possible, to minimize the relative energy required to vaporize the water channel and maximize target irradiation. This technical aspect differs from lasers with short pulse duration, where cavitation effects are maximized with a small separation distance.<sup>2</sup> Thus, short pulse lasers with photoacoustic properties fragment stones best when there is a small separation distance between the fiber and the stone to maximize vapor bubble expansion (and maximize collapse pressures) while, in contrast, long pulse



**Figure 33.2** Laser lithotripsy mechanism. The high-intensity acoustic shock wave developed by cavitation bubbles propagates from the laser fiber. The stone can fragment as a result of the pressure wave from the cavitation bubble.

lasers with photothermal properties fragment stones best when there is no separation distance between the fiber and the stone. Another practical implication of water absorption of holmium:YAG energy is that the depth of optical penetration through water is limited, implying a high safety margin.<sup>9</sup> Thus, even though holmium:YAG lasers have a greater risk of thermal injury to soft tissue compared to photoacoustic lasers, their

use in intracorporeal lithotripsy is safe as long as they are in contact with stones and there is at least 1 mm separation distance between the optical fiber tip and soft tissue.

As mentioned, holmium:YAG irradiation of urinary calculi causes fragmentation by a photothermal mechanism.<sup>5,10,11</sup> Fragmentation occurs when stones reach a critical temperature.<sup>5,12</sup> The orderly thermal diffusion produces symmetric surface craters, in contrast to other lithotripsy modalities.<sup>13,14</sup> In recent work, these craters were demonstrated to approximately grossly the fluence of the exiting beam.<sup>15</sup> As the gross configuration of the exiting optical beam is Gaussian, the lithotripsy craters more or less approximate this shape. In essence, the volume of stone irradiated with sufficient energy to raise that same volume to criterion threshold to produce lithotripsy is the only part of the stone that fragments. Thus, photothermal lithotripsy produces predictable and regular craters in contrast to photoacoustic lithotripsy. A practical difference is that resulting stone fragments are smaller for holmium:YAG lithotripsy compared to other lithotripsy modalities.<sup>16</sup> Regardless of stone composition, fragments produced by holmium:YAG lithotripsy are smaller than 1 mm in diameter. Since small fragments are produced, holmium:YAG lithotripsy is less efficient and proceeds at a slower rate compared to other modalities.<sup>11</sup> Thus, holmium:YAG lithotripsy is slower compared to photoacoustic lasers, but the resulting fragments from holmium:YAG lithotripsy are less likely to produce clinical problems such as colic or ureteral obstruction.

Holmium:YAG lithotripsy has an advantage compared to other lasers in that it effectively fragments all stone compositions.<sup>14</sup> Because pressure waves are much weaker with holmium:YAG compared to other modalities, there is little stone retropulsion or recoil.<sup>17,18</sup> Retropulsion occurs in holmium:YAG lithotripsy largely as a result of the force vector of fragments ejecting off the stone surface.<sup>19</sup> In an experiment, plume was seen to eject off the surface of an irradiated surface at right angles to the stone surface. Thus, wide shallow craters would tend to have more plume (stone fragments) ejecting at a right angle to the surface, producing greater retropulsion, compared to narrow deep craters. Since small-diameter optical fibers produce narrow deep craters, whereas large-diameter optical fibers produce wide shallow craters, retropulsion is minimal using small-diameter fibers. Given that retropulsion is minimal with the holmium:YAG laser using the small fibers commonly used for ureteroscopy, it is advantageous since large ureteral stones can be treated endoscopically, with little risk of retrograde displacement of calculi into the kidney.<sup>20</sup>

Holmium:YAG optical energy is transmitted using optical fibers. The low-OH silica optical fibers come in various diameters (365–940  $\mu\text{m}$ ). A smaller 272  $\mu\text{m}$  diameter optical fiber (SlimLine-200, Lumenis, Santa Clara, California) is composed of a doped silica mixture, which is more prone to thermal degradation and optical fiber damage.<sup>13,21</sup> A 200  $\mu\text{m}$  diameter optical fiber is also available (Innova, Phoenix, Arizona). The 365  $\mu\text{m}$  optical fiber is usually the fiber of choice for most ureteroscopic lithotripsy applications, unless the 200  $\mu\text{m}$  or 272  $\mu\text{m}$  optical fibers are required for flexible ureteroscopy.<sup>22</sup> Each of these fibers is an end-firing fiber, with the beam exiting the optical fiber at 0° orientation, or along the long axis of the optical fiber. With the advent of retrograde ureteronephroscopy, the use of the smallest fibers is increasingly important. A number of manufacturers produce holmium:YAG optical fibers ranging from 200 to 300  $\mu\text{m}$  diameter. At deflections and bending radii similar to retrograde ureteronephroscopy that would be used for lower pole stones, there are significant

differences in energy transmittance with these fibers. Some of the fibers do not transmit the energy well with such severe bending requirements, and can accumulate laser energy at the site of the bend, resulting in rapid optical fiber destruction at that site (fiber breaking into two pieces) with further energy transmission from the proximal bent fiber to the working channel of the ureteroscope.

To enhance irradiation efficiency, the optical fiber should be oriented so that the laser beam strikes the stone surface as close to 90° as possible. This perpendicular orientation enhances the photothermal mechanism. (An analogy is that during equinox, the sun's rays strike the equator's surface at 90° and the polar surfaces at 45°, with correspondingly different thermal effects for the same optical output.) Thus, the end-firing fibers should be oriented perpendicular to the stone surface. There are sidefiring (70°) fibers which are useful when the perpendicular orientation may be difficult to achieve, such as during percutaneous nephrolithotomy, where the percutaneous access tract does not typically provide a 'bull's-eye' target of the stone, or during cystolithotripsy of a large bladder calculus, where the optical fiber tends to orient tangentially towards the superior aspect of the stone.<sup>46,49</sup>

Since the holmium:YAG laser fragments stones through a photothermal mechanism, it is logical that the more energy per time (power) that can be transmitted to the stone, the more photothermal effect and the more efficient lithotripsy becomes. The corollary is that high energy and frequency settings (high power) ought to make lithotripsy fast. In reality, high power is not necessarily helpful and is potentially harmful. First, holmium:YAG optical fibers are susceptible to thermal degradation at pulse energies >1.0 J.<sup>13,21,34</sup> As fibers degrade, the optical output becomes less collimated, compromising efficiency and safety. Fiber degradation is greatest for calcium and struvite calculi. There is no apparent degradation with uric acid or cystine stone irradiation.<sup>34</sup> Secondly, pulse energies >1.0 J increase stone retropulsion, presumably due to increased pressure waves as the vapor bubble enlarges.<sup>17</sup> Retropulsion causes the stone to move away from the optical fiber, so that there is increased separation distance between the optical fiber and the stone surface. Irradiation is inefficient through water.<sup>7</sup> The urologist has to chase the stone, which is inefficient and frustrating. Thirdly, high pulse energies increase the width of the vapor bubble.<sup>23</sup> The vapor bubble represents boiling water, so a wide vapor bubble may potentially compromise safety, particularly during ureteroscopic lithotripsy, where accidental heating of the mucosa could occur. Thus, for most lithotripsy applications a low pulse energy and frequency are recommended at the outset (0.6 J at 6 Hz). If increased lithotripsy speed is desired, pulse energy may be increased to 1.0 J and frequency to 10 Hz. Additional lithotripsy speed is best obtained by increasing frequency but not pulse energy.<sup>34</sup>

A curious scientific sequela of photothermal lithotripsy is that holmium:YAG lithotripsy of uric acid calculi produces cyanide.<sup>12</sup> Uric acid undergoes thermal degradation to cyanide and alloxan.<sup>12,24</sup> Fortunately, there have been no reports of cyanide toxicity related to holmium:YAG lithotripsy. Since the minimal lethal dose of cyanide after oral ingestion is 50 mg, and it takes approximately 1 kJ of holmium:YAG irradiation of a pure uric acid calculus to produce 50 mg of cyanide, we infer a high safety margin. Most lithotripsy cases are completed with much lower energies, and irrigation throughout lithotripsy physically removes cyanide from potential absorption. The rate of cyanide absorption across urothelium is unknown. Presumably the urothelium

is a greater barrier to absorption than the gastrointestinal tract. Excess alloxan exposure is known to cause diabetes. To our knowledge, there are no known cases of diabetes as a result of holmium:YAG lithotripsy of uric acid stones, presumably due to similar issues above with cyanide (small alloxan dose, removal of alloxan in the irrigation, and urothelial barrier to absorption).

From the physics discussion, some advantages of holmium:YAG lithotripsy are obvious: optical energy may be transmitted through small-diameter flexible optical fibers (permitting their use in small-caliber flexible ureteroscopes), all compositions are effectively fragmented, small fragments are produced, little retropulsion occurs, and there is little risk of collateral mucosal injury. Thus, holmium:YAG lithotripsy is particularly attractive for ureteroscopic management of calculi. Most series show excellent stone-free outcomes from a single ureteroscopic session. An early report showed an 85% stone-free rate from a single ureteroscopic treatment, using a prototype holmium:YAG laser.<sup>25</sup> Later reports showed success rates of 90–98%.<sup>20,26,27</sup>

However, the definitive series was reported by Sofer et al, Canada.<sup>28</sup> This prospective study detailed a cohort of 598 patients whose renal ( $n=56$ ) and ureteral calculi were treated primarily with intracorporeal holmium:YAG lithotripsy. Patients were rendered stone free in 98%, 100%, and 97% of cases if their stones were in the distal, middle, and proximal ureter, respectively. In 94% of patients treated, they were rendered stone free from a single ureteroscopic procedure. In contrast, the stone-free rate for renal calculi treated by retrograde ureteronephroscopy and holmium:YAG lithotripsy was 84%. Fragmentation was incomplete in only 38 of 598 (6%) cases, of which 28 were large stones that migrated into the lower pole of the kidney. Quite simply, if you can visualize the stone endoscopically and place the holmium:YAG fiber onto the stone surface, you can fragment the stone successfully (Figure 33.3). These results underscore multiple other reports of smaller series, all of which show stone-free outcomes in greater than 90% of ureteral stone patients.<sup>20,25–27</sup>

Another issue raised by the study of Sofer et al was that only 24% of cases required balloon dilation.<sup>28</sup> In fact, ureteral orifice dilation reflected the authors' early experience, as they note fewer than 5% of cases currently require dilation. Further, only 72% of patients were stented postoperatively. Of the patients left unstented, none required restenting due to colic or sepsis. Favorable outcomes of unstented versus stented patients after ureteroscopy have been reported elsewhere.<sup>29–31</sup> It is likely that the tiny fragments produced by holmium:YAG lithotripsy permit easy passage of stone debris so that stenting is not routinely necessary. Further, the small caliber of semirigid and flexible ureteroscopes commonly used (6.8–7.5F) are comparable to ureteral stent diameters. Since there is no need to dilate the ureteral orifice for routine stent placement, it should come as little surprise that dilation may not be required for ureteroscopy. Another interesting observation



**Figure 33.3** Ureteroscopic stone lithotripsy with holmium:YAG lithotripsy. A safety guide wire is always used for ureteroscopic lithotripsy. Once the stone is visualized, the holmium:YAG laser fiber is placed onto the stone surface and fragmented.

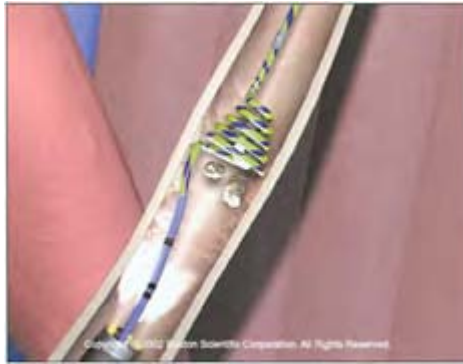
in the study by Sofer et al was that basketing was not routine: rather, the authors tended to fragment stones with holmium:YAG lithotripsy until all fragments were tiny enough to pass easily. Clinicians who wish to basket fragments may need to dilate the ureteral orifice if there is a risk of an impacted stone basket or ureteral avulsion.

Cheung et al reported treating 134 ureteral stones with holmium:YAG lithotripsy.<sup>32</sup> Of the ureteral stones, 31% were >10 mm and 69% were ≤10 mm. The mean sizes of the large and small stones were 15.4 mm and 7.7 mm, respectively. Large stones were more often located in the proximal ureter than small stones (49% vs 24%,  $p=0.001$ , respectively). Larger stones required longer anesthesia and surgical times compared to smaller stones, as expected. The overall stone clearance rate within 3 months without ancillary procedures was 93% vs 91%,  $p=0.8$ , respectively. Looking at stone clearance rates by ureteral location (proximal, middle, distal), they noted a trend. The stone clearance rate for large ureteral stones was better than for small ureteral stones in the proximal ureter (90% vs 64%,  $p=0.07$ , respectively.) In addition, the reason for failure in each of these smaller calculi was proximal migration: small stones are less likely to be impacted, and the irrigation used during ureteroscopy may risk pushing the smaller stone retrograde into the kidney. In a prior study, Teichman et al noted similar phenomena, with less retropulsion during holmium:YAG vs electrohydraulic lithotripsy.<sup>20</sup> An important point raised by the study of Cheung et al is that the authors did not have access

to small-caliber actively deflectable flexible ureteroscopes, which would have allowed them to chase the stones into the kidney easily. There are take-home points from this study. First, holmium:YAG lithotripsy yields effective stone-free clearance regardless of stone burden. Secondly, when dealing with smaller ureteral stones, several strategies are important to prevent or manage proximal migration. The table may be positioned in reverse Trendelenburg. A Dretler stone cone (Microvasive, Natick, Massachusetts) may be positioned proximal to the stone to prevent fragment migration (Figure 33.4). A flexible ureteroscope should be available so that if fragments do migrate proximally to the kidney (the lower pole especially), the stone may still be managed. For lower pole calculi, repositioning the table to Trendelenburg, and the use of tipless baskets and the smaller 272  $\mu\text{m}$  optical fiber are useful.

Most authors use low-energy and low-frequency settings (0.6 J at 6 Hz). Although higher power settings may deliver more energy to the stone and hence make lithotripsy proceed faster, fiber degradation and increased separation distance between fiber tip and stone surface limit the efficiency of fragmenting stones at pulse energy settings greater than 1.0 J.<sup>33,34</sup>

A risk during ureteroscopic holmium:YAG lithotripsy is accidental mucosal irradiation, causing thermal injury and stricture<sup>25</sup> (Figure 33.5) Devarajan et al noted 10 strictures after 300 ureteroscopic procedures, some of which may have been caused by inadvertent mucosal irradiation.<sup>27</sup> Grasso noted ureteral stricture in only one out of 63 patients, in whom a prior ureteral perforation and stone



**Figure 33.4** Microvasive Stone Cone™ nitinol retrieval device (courtesy of Boston Scientific Corp., Natick, Massachusetts). The Stone Cone nitinol retrieval coil is designed to sweep multiple stone fragments and prevent fragment migration.

impaction were present, raising the possibility that the larger risks for ureteral injury may be due to inflammatory reaction and ureteroscope trauma.<sup>26</sup> In the study by Sofer et al,<sup>28</sup>

only 4 laser-related complications from 598 patients (<1%) were noted. One ureteral perforation was seen, and 3 cases had laser fiber breakage within the ureterscope. The ureteral perforation was an early complication within the authors' experience, in which the optical fiber was not visualized when laser energy was discharged. This complication is noteworthy as the holmium:YAG laser should only be fired when the fiber tip can be visualized in contact with the stone surface. Judicious irrigation is



**Figure 33.5** Ureteral stricture. Thermal injury from prior ureteroscopic holmium:YAG lithotripsy can lead to stricture.

helpful to facilitate visualization, as the tiny stone fragments from holmium:YAG lithotripsy can obscure endoscopic vision.<sup>35</sup> The 3 cases with laser fiber breakage within the ureterscope are noteworthy, since, if unrecognized, this situation could lead to laser transmission to the ureterscope itself, with thermal destruction to the ureterscope. It bears repetition that the laser should only be fired when the optical fiber tip can be



visualized. Further, the laser fiber should be inspected prior to use in the darkened operating room with the tracer beam on in order to determine if light 'leaks' along the fiber. Such a light leak would indicate a fracture of the fiber, with the risk of transmitting laser energy to the ureterscope or errantly within the operating room. In an ex-vivo study which compared holmium:YAG versus pulsed dye laser and electrohydraulic and pneumatic lithotripters, the holmium:YAG laser had the lowest safety margin for ureteral perforation.<sup>36</sup> In that study, the lithotripters were placed at a right angle to ureteral mucosa, unlike most scenarios of clinical lithotripsy. Because irradiation effects are directly related to energy density, and energy density is lowest at tangential orientation between the incident laser beam and target mucosa, ureteroscopic holmium:YAG lithotripsy generally carries a high safety margin.<sup>9,37</sup> However, if the laser is discharged with the optical fiber tip in contact with ureteral mucosa, thermal injury and perforation may nonetheless result. Accidental mucosal irradiation and perforation are unlikely with a separation distance greater than 1 mm at a tangential orientation or greater than 2 mm at a right-angle orientation.<sup>9,36</sup> Thus, it is imperative that holmium:YAG lithotripsy be performed only as long as the urologist can visualize the optical fiber tip in contact with the stone surface. Because holmium:YAG fragments are small, the endoscopic appearance during lithotripsy has been described as a 'snowstorm', so that adequate irrigation is required or else endoscopic vision may be obscured by fragments.<sup>26</sup> During ureteroscopy, the use of pressure irrigators is recommended to maintain endoscopic vision during holmium:YAG lithotripsy and to minimize heat accumulation.

Since holmium:YAG optical fibers are small caliber, small (6–7F) ureteroscopes may be used. These small ureteroscopes can often be passed easily in the undilated ureteral orifice and holmium:YAG lithotripsy performed until complete stone fragmentation. The tiny fragments will usually have already passed into the bladder with the irrigation, or the small residual calculi will pass easily. Some authors extend this same principle to justify not stenting, and save the patient the morbidity of the ureteral stent.<sup>38,39</sup> However, if stone fragments are to be collected for stone analysis and basketing is anticipated, we recommend ureteral dilation and stent placement. Additionally, if a prolonged ureteroscopy is anticipated, with multiple passes of the flexible ureterscope in and out of the ureter, a ureteral access sheath placed during the procedure to facilitate repetitive passage of the ureterscope, and a stent placed at the conclusion of the procedure.

The small instrumentation permits holmium:YAG lithotripsy in pediatric patients. In one series, 5 of 8 children were rendered stone free in one procedure using both retrograde and antegrade approaches.<sup>40</sup> In another series, 16 of 19 children (84%) were rendered stone free in one procedure.<sup>41</sup> In both series, no holmium:YAG-related complications were noted. Additionally, a total of 19 children in these two studies were imaged postoperatively to exclude ureteral stricture and none of these patients had evidence of stricture. These negative observations are important, since there is the increased potential risk of thermal injury in the small pediatric anatomy.

Although rarely an issue, the urologist may occasionally encounter stone patients with bleeding diatheses. Because of the paucity of acoustic pressure effects there is minimal risk of collateral damage to mucosa. For this reason, ureteroscopic holmium:YAG lithotripsy can be safely performed in patients with bleeding diathesis, sometimes without stopping anticoagulation.<sup>42</sup> Another unusual situation is treating renal calculi in the morbidly obese patient. Andreoni et al reported on the use of flexible ureteroscopy for

proximal ureteral and renal calculi in morbidly obese patients, whose obesity precluded shock wave lithotripsy.<sup>43</sup> Eight patients underwent 10 ureteroscopic procedures. The average stone size was 11 mm. Of the 10 procedures, holmium:YAG lithotripsy was used in 8, electrohydraulic lithotripsy was used in 4, and pulsed dye lithotripsy used in 1 procedure. Seven patients (70%) were rendered stone free after a single treatment. Of the 8 patients treated with holmium:YAG lithotripsy, 7 (88%) were stone free and treated as outpatients. The one failure of holmium:YAG lithotripsy had a 10 mm left lower calyceal stone, rendered into 5 mm and 3 mm fragments in a middle calyx. The patient stayed 1 day postoperatively. These results compare favorably to what one would expect for shock wave lithotripsy or percutaneous nephrolithotomy in the morbidly obese population. Shock wave lithotripsy in this setting is difficult, as stone targeting may not be possible if the stone is poorly imaged as a result of body habitus or due to inability to bring the stone in the F2 position. Percutaneous nephrolithotomy in this population may be challenging as access is limited due to obesity, and increased fluoroscopy is required. The authors state that ureteroscopic holmium:YAG lithotripsy is their first-line therapy for renal calculi up to 2 cm in size in the morbidly obese population. Although no randomized studies have been reported to date to specifically address this population, it seems reasonable to offer ureteroscopy in this setting as first-line therapy when shock wave lithotripsy is likely to be unsuccessful.

Holmium:YAG lithotripsy may be used for renal calculi either with retrograde ureteronephroscopy or with percutaneous nephrolithotomy. For retrograde ureteronephroscopy, the main advantage of holmium:YAG is that the 272  $\mu$ m optical fiber offers enhanced endoscope deflection, so that even the lower pole may be accessed by retrograde endoscopy.<sup>21,22,26,44</sup> An obvious advantage of this approach is that it is minimally invasive. A disadvantage of this approach, however, is that it is time consuming and may be technically challenging. It is essential that the optical fiber be passed through the straightened ureteroscope so that the fiber tip is beyond the ureteroscope.<sup>26</sup> The ureteroscope and fiber tip may then be deflected. If the optical fiber is passed after the ureteroscope is deflected, the working channel narrows and the fiber tip may perforate and damage the ureteroscope working channel, making further use of the ureteroscope impossible. Several maneuvers may facilitate retrograde ureteronephroscopic access to the lower pole of the kidney. First, if the patient is placed prone with the head down, the angle between the axis of the renal pelvis and the lower pole infundibulum increases, permitting easier access to the lower pole with retrograde ureteronephroscopy.<sup>45</sup> A potential disadvantage of prone ureteroscopy is that most urologists are not familiar with cystoscopic landmarks in the prone position, so that initial ureteral access may be difficult. Another technique would be to pass the flexible ureteroscope into the renal pelvis, and, with the ureteroscope straight, pass stone-grasping forceps just beyond the ureteroscope; then, deflect and advance the ureteroscope into the lower pole, engage the stone in the forceps, and reposition the stone into the renal pelvis or upper pole. Exchange the forceps for the holmium:YAG optical fiber and the stone may be fragmented in the renal pelvis or upper pole, so that ureteroscopic access is easier than if the stone were left in the lower pole. This technique should be reserved for a large stone, since if a small lower pole stone can be engaged into a tipless nitinol basket, the easiest maneuver would be to remove the stone in the basket and obviate lithotripsy.

An additional caveat to retrograde ureteronephroscopy and endoscopic lithotripsy is that the optical fiber tip must be visualized to exit the ureterscope, and the tip verified to be at least several millimeters away from the ureterscope, before discharging holmium:YAG energy. Inadvertent holmium:YAG discharge with the optical fiber tip within the ureterscope or close to the ureterscope will readily damage (or destroy) the ureterscope. As mentioned in the laser physics discussion, some small-caliber optical fibers do not transmit holmium:YAG energy when in maximal deflection ( $180^\circ$ ) and with a tight bending radius. It bears repetition that the urologist must be cautious during retrograde ureteronephroscopy should the fiber break and irradiation proceed to the working port of the ureterscope.

Percutaneous nephrolithotomy may be performed with the holmium:YAG laser.<sup>25,46</sup> Since holmium:YAG fragments slowly, several potential strategies may be used to increase lithotripsy efficiency. A large-caliber fiber ( $550\ \mu\text{m}$  or  $940\ \mu\text{m}$ ) may be used and the pulse energy increased. Even better, the use of angled delivery systems ( $70^\circ$   $550\ \mu\text{m}$  optical fiber) allows enhanced coupling of the optical beam to the stone surface. The key advantage here is that the energy density is maximized with a right-angle orientation between the laser beam and the stone surface ( $0^\circ$  laser incident angle). Increased energy density yields efficient lithotripsy speed.<sup>13</sup> Another reason to consider holmium:YAG lithotripsy for renal calculi is that the photothermal mechanism is bactericidal when fragmenting struvite calculi.<sup>47</sup>

The larger question is not whether holmium:YAG lithotripsy may be used for renal calculi, but when should it be used for renal calculi. Most urologists would choose to do shock wave lithotripsy for renal calculi  $<2\ \text{cm}$  not in the lower pole (assuming that stone composition is not known, or that composition is known not to be monohydrate, cystine, or brushite). Thus, other calculi or patients who have already failed shock wave lithotripsy might be indications for retrograde ureteronephroscopy or percutaneous nephrolithotomy. For most urologists, large stone burden is best managed with percutaneous nephrolithotomy, starting first with ultrasonic lithotripsy. Ultrasonic lithotripsy has a high safety margin and is effective for most compositions. The ability to fragment and evacuate debris is advantageous. Pneumatic lithotripsy is also useful, given the rapid fragmentation. The disadvantage is the need to chase, grasp, and remove large fragments. The newer combined pneumatic-ultrasonic lithotripsy devices are more efficient, particularly for large renal stones treated by percutaneous nephrolithotomy. Holmium:YAG lithotripsy is useful in percutaneous nephrolithotomy for stones which do not fragment to other modalities or to incorporate flexible nephroscopy to pursue stones in the collecting system which cannot be accessed with rigid nephroscopy and ultrasonic lithotripsy. Thus, flexible nephroscopy and the holmium:YAG laser may permit the entire collecting system to be accessed through a single nephroscopy tract, obviating the need for multiple percutaneous tracts. For 8 patients with a mean preoperative renal stone burden of  $48\ \text{mm}$ , the stone-free outcome for a single session of holmium:YAG percutaneous nephrolithotomy using the  $70^\circ$  angled optical fiber was  $88\%$ .<sup>46</sup> Retrograde ureteronephroscopy may be considered for patients who do not want percutaneous nephrolithotomy or who could not tolerate prone positioning. Because of the small instrumentation, these cases may be challenging. Stones less than  $1\ \text{cm}$  may be the best indication to consider the retrograde approach, since larger stones are time consuming. The stone-free outcome for a single session with retrograde ureteronephroscopic

lithotripsy using the holmium:YAG laser is 60–79%.<sup>44,48</sup> In one study using this technique for renal calculi  $\geq 2$  cm, including minor staghorn calculi, the authors reported that 91% of renal calculi were completely pulverized (defined as fine dust and fragments  $< 2$  mm).<sup>44</sup> Nonetheless, secondlook endoscopy revealed residual fragments requiring additional holmium:YAG lithotripsy in 53% of cases. Thus, urologists who wish to use the retrograde ureteronephroscopic approach should consider carefully if they feel comfortable doing a prolonged ureteroscopy procedure, and if the patient is willing to accept the potentially increased likelihood of a second ureteroscopy to render the patient stone free.

Bladder calculi are particularly amenable to holmium:YAG lithotripsy. The bladder poses a unique problem for other lithotripsy modalities insofar as calculi tend to move within the bladder during lithotripsy. The lack of retropulsion implies that the urologist can irradiate a bladder calculus continuously without having to stop and chase the stone around the bladder.<sup>49</sup> Further, the tiny fragments are easily removed with an Ellik evacuator, so that grasping forceps or baskets are unnecessary. Success rates for single-session monotherapy should approach 100%.<sup>25,26,49</sup> Similar to renal calculi approached percutaneously, the use of angled delivery systems (70° 550  $\mu$ m optical fiber) permits efficient coupling to attain as close to a normal incidence as possible, and achieve maximal energy density and enhanced lithotripsy speed. We have found that the use of the angled optical fiber is easy and efficient, with attention to keeping the optical aperture (the 'hole' at the side of the optical fiber tip through which optical energy is transmitted) oriented to the stone, to minimizing the separation distance between this aperture and the stone surface, and to creating a cavity within the stone. Once a cavity is created, the optical fiber can be inserted into the cavity, and the optical fiber rotated within the cavity to 'resect' the stone. By using the stone as a shield, there is little risk of accidental pass-point and mucosal irradiation. In general, even bladder calculi as large as 6 cm can be completely fragmented and evacuated in under 1 hour, making this minimally invasive approach advantageous to open cystolithotomy, both for morbidity and operative time.<sup>49</sup>

When end-firing fibers are used, a 550  $\mu$ m or 940  $\mu$ m optical fiber should be used and passed through a ureteral catheter within the working channel. These technical points will facilitate fiber stiffness and stabilization. Smaller optical fibers (and omission of the ureteral catheter) tend to be floppy and limit the surgeon's control of the optical fiber.

Photoacoustic laser lithotripsy is also effective for urinary calculi. The pulsed dye laser was effective at stone fragmentation for all compositions except calcium oxalate monohydrate and cystine. Fragmentation improved using a 320  $\mu$ m diameter fiber at high pulse energy compared with using the smaller 200  $\mu$ m fiber, which restricted pulse energy.<sup>50</sup> The regular lattices of these compositions produced stable structures presumably, so that the pressure transients produced from the pulsed dye laser were not always sufficient to fragment these stones. Cystine also does not absorb the 504 nm wavelength.<sup>51</sup> All other stone compositions absorb this wavelength. Nonetheless, clinical success rates ranged from 80–95%.<sup>52</sup> The pulsed dye laser has largely been replaced by the holmium:YAG laser, as the latter effectively fragments all stone compositions, and does not have maintenance costs as high as the pulsed dye laser (the coumarin green dye must be replaced periodically). Alexandrite lithotripsy is not widely used, partly due to its lack of fragmentation efficacy for cystine and calcium oxalate monohydrate calculi, and partly due to the difficulty with optical fiber breakdown.<sup>53,54</sup> In the study by Pearle et al,<sup>53</sup>

alexandrite lithotripsy was effective for small ureteral stones, but less effective for stones larger than 10 mm or stones in the kidney. In the study by Denstedt et al,<sup>54</sup> this laser failed to fragment calculi in 50% of cases.

An interesting practical problem associated with pulsed dye and alexandrite lasers is the protective laser safety eyewear (LSE) devices that must be worn during use. LSE devices must be worn using all medical lasers, in case of accidental ocular exposure to laser energy. However, since pulsed dye ( $\lambda=504$  nm) and alexandrite lasers ( $\lambda=755$  nm) emit in the visible wavelengths, the LSE devices block visible light from the urologist's eye, creating color distortion and impaired perception of the surgical field.<sup>55</sup> Because holmium:YAG operates at 2100 nm, above the visible spectrum, there is little color distortion created with LSE devices to block holmium:YAG wavelengths.

Currently, some new lasers have been described and show promise. The frequency (FREDDY) laser is effectively a short-pulse duration laser with photoacoustic properties.<sup>56</sup> This laser emits both at 532 nm and at 1064 nm to create a plasma on the stone. Similar to the experience with the pulsed dye laser 15 years ago, the FREDDY laser fragments stones of calcium oxalate dihydrate and struvite compositions well, but does not fragment cystine stone compositions consistently. In the initial report, no calcium oxalate monohydrate stones were included. This laser is currently undergoing clinical testing and may be attractive on the basis of cost and safety, but it remains to be seen what advantages it provides over existing lasers. Another laser of interest is the erbium:YAG laser; its wavelength ( $\lambda=2900$  nm) is more effectively absorbed by stones compared with the holmium:YAG wavelength. The efficient energy absorption by the stone implies more efficient fragmentation. Preliminary work with free electron laser systems validated larger ablation craters using the 2900 nm vs 2100 nm wavelength.<sup>57</sup> In some in-vitro work, erbium:YAG lasers were more efficient than holmium:YAG lasers for lithotripsy.<sup>58</sup> These experiments were done with relatively low pulse energy (100 mJ). Current experiments are being conducted with higher pulse energies to determine if erbium:YAG remains advantageous at higher pulse energies.

### **Holmium:YAG soft tissue applications**

Similar to lithotripsy, many current urologic soft tissue laser applications are performed successfully using the holmium:YAG laser.<sup>59,60</sup> Nonetheless, Nd:YAG, KTP, (potassium titanyl phosphate) and diode lasers have been used for urologic soft tissue applications, too. And some recent reports using erbium:YAG lasers suggest a potential utility.

For soft tissue, the holmium:YAG laser is well absorbed in water with a penetration depth of less than 0.5 mm, so there is a predominant vaporization effect as energy is concentrated in a shallow volume (high fluence).<sup>7</sup> Indeed, immediate tissue ablation or vaporization from holmium:YAG is the predominant effect on the prostate.<sup>61</sup> Kabalin showed that ablation craters in dog prostate from contact holmium:YAG ablation were predominantly caused by vaporization, with craters as wide as 2 cm. There was a small rim peripheral to the ablation crater where coagulation occurred. In contrast, continuous Nd:YAG irradiation ( $\lambda=1064$  nm) has greater tissue penetration, larger scatter, and decreased fluence, with resulting predominant thermal injury and coagulation.<sup>62</sup> The decreased fluence and greater tissue penetration occur as a result of the minimal

absorption by water and body pigments. Thus, little vaporization occurs unless high-energy irradiation is performed for a prolonged period of time. In a study of dogs treated by Nd:YAG contact ablation, serial changes in the prostate histology were reported at 1 and 3 hours, at days 2, 4, and 7, and at weeks 2, 3, 5, and 7 postoperatively.<sup>63</sup> At 1 and 3 hours, tissue disruption and hemorrhage separate a central coagulative necrosis from normal peripheral zone tissue. By day 1, this coagulation zone shows multiple areas of cavitation. In the ensuing weeks, these areas coalesce and form a large central cavity. By day 7, this central cavity is lined by a narrow zone of necrosis with macrophages and neutrophils. By 5 and 7 weeks, the central cavity is lined by transitional epithelium. These results demonstrate the thermal injury and delayed slough. Similar thermal injury, coagulation necrosis and liquefaction changes are seen with interstitial delivery of Nd:YAG optical energy.<sup>64,65</sup>

The KTP laser is an Nd:YAG laser where the 1060 nm optical output is passed through a KTP crystal, producing a wavelength emission at 532 nm. At this wavelength, the vaporization and coagulation effects are intermediate between those observed for Nd:YAG and holmium:YAG lasers. The KTP wavelength is highly absorbed by hemoglobin, making it particularly advantageous for treating cutaneous and urethral hemangiomas.<sup>66</sup> Diode lasers are a class of laser device that are small, portable, and generally less expensive than conventional laser devices. The indigo laser is a diode laser ( $\lambda=830$  nm) that uses a diode pump and gallium-aluminum-arsenide as the excitable medium. At this wavelength, diode lasers have similar tissue interactions to the Nd:YAG laser.<sup>67,68</sup>

Comparison of results from Nd:YAG ablation of the prostate is difficult due to variations in delivery systems, power settings, and techniques. Nd:YAG ablation has been described using end-firing and side-firing fibers. Kabalin demonstrated that maximal ablation volumes were achieved with contact Urolase (CR Bard, Inc., Covington, Georgia) right-angle firing Nd:YAG ablation at 40 W for 90 s.<sup>62</sup> In a clinical study, Kabalin reported on 13 men with BPH (benign prostatic hyperplasia) treated with the same laser parameters.<sup>69</sup> His group reported on a 5-year followup, noting that 2 patients were retreated for residual tissue, and 8 of the original 13 patients were evaluable at 5 years.<sup>70</sup> Of this cohort, the mean estimated preoperative excess prostate volume was 23 g. Comparing mean preoperative to mean 5-year outcomes, peak flow rates improved from 9 m/s to 22 m/s, residual volume decreased from 153 ml to 90 ml, and AUA (American Urological Association), symptom score decreased from 24 to 6. In another study, Kabalin et al compared men with symptomatic bladder outlet obstruction due to BPH. Men were randomized to standard transurethral electrocautery resection (TURP) versus Urolase right-angle firing Nd:YAG ablation.<sup>71</sup> They used slightly different Nd:YAG settings, applying contact ablation at 40 W for 60 s (as opposed to 90 s) at 3 and 9 o'clock positions, and 30 s at 6 and 12 o'clock positions. Comparing mean preoperative to 18-month results for TURP vs laser cohorts, peak flow rates improved from 9 ml/s to 21 ml/s vs 9 ml/s to 20 ml/s; residual volumes decreased from 291 to 143 ml vs 236 to 154 ml; and AUASS decreased from 19 to 6 vs 21 to 6, respectively. Two important differences were noted, however. The postoperative mean catheterization times were 3 days for TURP vs 5 days for laser. And the mean prostate volume at 1 year follow-up measured by transrectal ultrasound showed a decrease in volume of 59% for TURP vs 28% for laser. In a multicenter study, 115 men were randomized to transurethral

electrocautery resection versus Nd:YAG contact ablation.<sup>72</sup> Symptom score and peak flow rate changes were comparable. However, reductions in residual volume and quality of life favored transurethral electrocautery resection.

An interesting follow-up study treated a cohort of men with the same delivery system but applied 60 W power for 60 s in four quadrants. The intent was to ablate a greater volume of tissue at higher power and, by inference, achieve greater prostate volume reduction and clinical durability. Of 50 patients, 6 developed bladder neck contractures.<sup>73</sup> Based on the dosimetry studies, 40 W power may be better than 60 W, in part because of the charring at higher power.<sup>62</sup> Charring changes tissue characteristics, so that energy transmission is decreased, and a smaller volume of tissue is coagulated. Similarly, even at 40 W power setting, a plateau phase of tissue effects is achieved at 90 s irradiation. No further coagulation or ablation volume is achieved with additional irradiation.

Contact Nd:YAG prostate ablation is generally associated with prolonged postoperative catheterization times.<sup>71,73,74</sup> This complication has generally been attributed to a delayed slough. Although clinical efficacy may eventually be achieved with durable response, irritative voiding symptoms persisting greater than 4 months postoperatively may occur in over 10% of patients.<sup>75</sup> In a review article, Bosch compared published results of various treatments for bladder outlet obstruction from BPH based on urodynamic criteria.<sup>76</sup> Open prostatectomy was superior to standard TURP, followed by Nd:YAG laser prostatectomies. Stein reviewed 4 randomized studies comparing Nd:YAG contact ablation using a right-angle fiber delivery system versus standard TURP.<sup>74</sup> Overall, symptom scores and urinary flow rates improved for laser ablation, but less than occurred for standard TURP. Thus, the overall experience with contact ablation using Nd:YAG lasers has been improvement in obstructive voiding parameters, but at a cost of prolonged postoperative urinary retention, delayed slough, and irritative voiding symptoms.

Concerned that contact Nd:YAG laser prostatectomy was not ablating sufficient tissue to relieve obstruction as effectively as standard TURP, a number of trials were conducted with interstitial Nd:YAG ablation of the prostate. The objective was to create multiple zones of ablation, necrosis, and slough, but to effect a greater volume reduction than could be achieved by contact ablation techniques. Several articles showed modest flow rate improvements and modest symptom score reductions, generally less successful than the contact Nd:YAG techniques.<sup>77,78</sup> An advantage of this interstitial technique is that the procedure may be conducted on an outpatient basis, using only local anesthesia or sedoanalgesia. A disadvantage is that with greater volumes of coagulation necrosis, patients may expect prolonged catheterization times, so that most patients will wear a urethral catheter for at least 7 days, and prolonged dysuria is common.

Due to prolonged catheterization, delayed slough, and prolonged irritative voiding symptoms, lasers other than Nd:YAG were tried for prostate ablation. Experience with KTP for prostate ablation has been limited. In one study, 10 patients were treated with 60 W power setting with variable total energy (61–175 kJ).<sup>79</sup> The mean preoperative prostate volumes were 38 ml, AUA symptom scores were 19, and peak flow rates were 8 ml/s. At 3 months follow-up, mean AUA symptom scores were 4, and peak flow rates were 22 ml/s. The authors noted immediate vaporization defects and all catheters were removed on postoperative day 1. However, mean post residual volume did not change (148 ml vs

163 ml, pre- vs postoperatively, respectively,  $p=0.77$ ). A limitation common to all of these coagulation techniques is the difficulty in obtaining pathologic specimens.

Diode lasers have also been used for interstitial ablation of the prostate, similar to Nd:YAG interstitial ablation techniques. The advantage of the diode approach is that the laser is small, portable, and inexpensive. Several reports indicate that voiding parameters improve.<sup>80–83</sup> Symptom scores improved 50–70%. Peak flow rates postoperatively ranged from 14 to 17 ml/s. However, the study by Daehlin et al<sup>83</sup> reported results where peak flow rates improved modestly (8.6 ml/s preoperatively to 9.9 ml/s at 1 year), and residual urine volumes were unchanged. Importantly, postoperative perineal pain was reported by 72% of patients lasting 1–2 weeks.

Initial clinical use of holmium:YAG prostate irradiation was modeled after techniques used for Nd:YAG. Thus, the standard technique was to perform a visual laser ablation of the prostate (VLAP) using holmium:YAG irradiation in contact mode in an attempt to 'paint' the surface of the prostate.<sup>84,85</sup> This approach provided poor results, presumably due to the minimal tissue loss caused by holmium VLAP. Typically, a satisfactory endoscopic appearance at the end of the procedure, that an adequate channel had been created, was in reality minimal tissue loss.<sup>85</sup> Since there was minimal delayed slough, no further improvement could be expected, and patients typically failed.

However, the procedure has evolved such that the holmium:YAG laser is used to enucleate the prostate rather than do a VLAP.<sup>84,86–89</sup> The objective is to vaporize incisions and detach the adenoma from the surgical capsule, in order to enucleate the adenoma. The technique is to use the 550  $\mu$ m end-firing fiber through a 6F open-ended ureteral catheter and both through the working channel of the resectoscope. Incisions are made at 5 and 7 o'clock at the bladder neck and extended distally to the verumontanum. Laser settings of 2.5 J at 25–30 Hz are typical. The incision is then extended transversely at the verumontanum to undermine the floor of the prostate and effectively detach the median lobe from the capsule. The lateral lobes are then detached by undermining. The right lateral lobe is incised from 7 o'clock to 11 o'clock. The left lateral lobe is incised from 5 o'clock to 1 o'clock. Transverse incisions may be made to resect smaller pieces from the lateral lobe, if the adenoma is large. At the end of the procedure, the large pieces must be extracted from the bladder. Either a modified resectoscope loop (modified to make grabbing the tissue easy) or a tissue morcellator may be used. Although the dual-wavelength laser (holmium and neodymium) is commonly used, Nd:YAG irradiation for hemostasis should be avoided since it tends to promote dysuria, delayed slough, and prolonged catheterization.<sup>90</sup>

A recent study showed comparable postoperative outcomes with 1 year follow-up from standard TURP and holmium:YAG laser prostatectomy, among 120 men randomized prospectively.<sup>91</sup> There were equivalent reductions in AUA symptom scores, but greater improvements at 1-year follow-up for men treated by laser vs standard TURP for peak flow rates and quality of life. Fewer sideeffects were encountered in the holmium group: specifically, fewer blood transfusions and recatheterizations. In the study by Matsuoka et al, where nonrandomized patients were treated either by holmium:YAG prostatectomy or TURP, similar advantages of holmium:YAG were reduced bleeding and postoperative catheterization time.<sup>86</sup> Advantages of TURP over holmium prostatectomy were increased tissue retrieved and decreased resection time (mean 25 min vs 42 min, respectively). Gillig's group published a follow-up study of their same prospectively



randomized patients, with 2-year follow-up available in 86 of their initial 120 patients.<sup>92</sup> Equivalent improvements in AUA symptom score, peak flow rates, and quality of life scores were achieved with either technique. Comparing standard TURP vs holmium resection, respectively, mean catheter times were 37 hours vs 20 hours,  $p<0.001$ , and mean hospital stays were 48 hours vs 26 hours,  $p<0.0001$ . The holmium:YAG prostatectomy technique has a steep learning curve, although, once mastered, large glands may be safely treated endoscopically. Essentially, the holmium:YAG laser is used to enucleate the prostate in a retrograde fashion, with separate median and lateral lobe enucleations yielding large pieces. Initial attempts with this technique had the problem of trying to remove these large pieces from the bladder. However, a tissue morcellator may be used cystoscopically to remove large adenomatous pieces from the bladder.<sup>93</sup>

Holmium:YAG prostatectomy is also indicated for men in urinary retention. In one study of 36 men in urinary retention, the 6-month postoperative mean peak flow rate and AUA symptom score were 23 ml/s and 5.7, respectively.<sup>94</sup> The overall rate of recatheterization was 6%. Unlike prior lasers (Nd:YAG, KTP, diode) where coagulation necrosis limited the amount of tissue that might be debulked, the holmium:YAG prostatectomy can be applied to any sized prostate. Successful results have been achieved for adenomas over 100 g.<sup>95,96</sup> In the study by Kuntz et al, 120 patients with prostate volumes  $>100$  ml were randomized prospectively to holmium resection vs open prostatectomy. The baseline symptom scores, flow rates, and residual volumes were statistically equivalent. With 6-month follow-up, the respective improvements in AUA symptom scores (2.4 vs 2.8,  $p=0.61$ ), mean peak flows (30 ml/s vs 27 ml/s,  $p=0.11$ ), and residual volumes (4.4 ml vs 2.1 ml,  $p=0.40$ ) were equivalent. Comparing the holmium and open prostatectomy groups, mean operation times were 136 min vs 91 min,  $p<0.0001$ , mean hemoglobin loss was 1.9 g/dl vs 2.8 g/dl,  $p<0.0001$ , mean postoperative catheter durations were 31 hours vs 194 hours,  $p<0.0001$ , and mean postoperative stays were 70 hours vs 251 hours,  $p<0.0001$ , respectively.

The obvious issue is whether holmium:YAG laser prostatectomy competes successfully against standard TURP. There are advantages and disadvantages to both techniques. First, some degree of vaporization in performing a holmium:YAG prostatectomy results in tissue loss compared to TURP and retrieved tissue from holmium:YAG prostatectomy shows thermal artifact.<sup>84,86</sup> It is possible that incidental prostate cancer might be missed. In fact, the only 7 cases of prostate cancer found in one series were entirely in the TURP cohort in Gilling's randomized study.<sup>91</sup> Secondly, holmium:YAG prostatectomy takes longer to perform than TURP, even in experienced hands. Urologists not familiar with the holmium:YAG prostatectomy technique should not expect that they could perform this procedure without practice or without experiencing a learning curve. There were no gross differences in continence, potency, or adverse events. These encouraging results at 1-year follow-up suggest that holmium:YAG prostatectomy may compete with TURP as the 'gold standard' for surgical management of BPH. Clearly, the decreased catheter and hospital times and reduced blood loss and transfusion rates argue in favor of holmium:YAG prostatectomy. Longer-term follow-up and other reports will be important to assess the impact of potentially missing prostate cancer (in an era of PSA-driven biopsies), acceptance of a new technique, and willingness of providers to purchase a high-powered (80 W) holmium:YAG laser, typically in excess of \$140,000. Despite the high costs,

holmium:YAG prostatectomy may be more cost-effective than standard electrocautery resection, due to lesser postoperative care requirements.<sup>97</sup>

Holmium:YAG transurethral incision of the prostate may be performed where resection is not required. Holmium:YAG prostate incision may be performed successfully as a day surgery, with minimal blood loss, and catheter removal in the recovery room.<sup>98</sup> Similar to standard endoscopic prostate incision, there is a risk of infection and retrograde ejaculation.

Due to its predominant vaporization effect and minimal coagulation, the holmium:YAG technique is ideal for incisional applications and upper tract applications, where the effects of thermal coagulation would not be desirable. Davis et al initially described that an incised ureteral stricture can regenerate and epithelialize.<sup>99</sup> The holmium:YAG laser may be used to perform endoureterotomy,<sup>100–103</sup> where it may prove attractive as the energy source, since the predominant vaporization and minimal coagulation should yield minimal rescarring compared with alternate energy sources with predominant coagulation effects. In the largest series published to date, an overall 76% success rate was described.<sup>100</sup> All failures showed evidence of resticture within 3 months of the procedure. In the series by Singal et al,<sup>100</sup> holmium:YAG laser endoureterotomy was performed using a 6.9 semirigid ureteroscope for retrograde endoureterotomy of distal and middle ureteral strictures and a 9.8F flexible ureteroscope for retrograde endoureterotomy of proximal ureteral strictures or antegrade endoureterotomy. In all cases, a 400  $\mu\text{m}$  fiber was used. Following laser endoureterotomy, balloon dilation was performed and the ureter was stented. The total procedure time averaged 58 min for retrograde procedures and 120 min for antegrade procedures. Given that large total energy is required for these cases, it will undoubtedly be easier to control the optical fiber using the larger (365  $\mu\text{m}$ ) optical fiber, unless access requires the use of the smaller (272  $\mu\text{m}$ ) fiber. In another report, the authors were unable to visualize the stricture using this fiber, presumably because of decreased irrigation flow.<sup>101</sup> They were, however, successful using a smaller fiber. Although these results are encouraging, it is apparent that ureteroscopic endoureterotomy is technically demanding. Further, no published data exist to compare fluoroscopic retrograde endoureterotomy (Acucise endoureterotomy) with endoscopic holmium:YAG endoureterotomy.<sup>104</sup> As an aside, the erbium:YAG laser has even more precise ablation characteristics of soft tissue than the holmium:YAG laser, and so the erbium:YAG laser might prove to be more effective and safer than holmium.<sup>105</sup>

The holmium:YAG laser may be used to resect or ablate transitional cell tumors either in the bladder or the upper tracts. Large papillary bladder tumors may be incised at the base to detach the tumor from the bladder. Typically, an end-firing fiber is used. Use of the laser in this fashion does not appear to affect the ability to stage the tumor accurately.<sup>106</sup> Hemostasis may be obtained by irradiating bleeding points with the optical fiber tip just off contact from the mucosa. With a small separation distance between the optical fiber and the mucosa, the laser irradiates the water, and the irradiated water superheats. This technique, called 'defocusing', permits the urologist to choose between vaporization (contact mode) and coagulation (noncontact mode). Alternatively, the dualwavelength laser (Lumenis VersaPulse Select) permits Nd:YAG irradiation, which produces more coagulation than the holmium:YAG laser. Note that the depth of penetration of the Nd:YAG laser is greater than that of the holmium:YAG laser, and

excessive Nd:YAG irradiation in the bladder could produce bowel injury adjacent to the irradiated bladder, even with an intact bladder. Dosimetry studies of Nd:YAG ablation show that bowel perforation from bladder irradiation is unlikely to occur using 30 W power for no more than 15 s, or 10 W power for no more than 30 s.<sup>107</sup> With these low powers in mind, Rofeim et al treated 24 interstitial cystitis patients with Runner's ulcers, ablating their bladder ulcers successfully with 15 W power for no more than 3 s.<sup>108</sup>

Upper tract transitional cell carcinoma may be treated ureteroscopically with holmium:YAG irradiation, too. Typically, 1.0–1.5 J pulse energy at 5–10 Hz frequency is used.<sup>42,48</sup> Papillary lesions may be irradiated at their base to resect the lesion from the urothelial mucosa. The freefloating lesion is grasped and removed. Alternatively, the lesion may be ablated. If the diagnosis is uncertain or pathology is desired, use of a 3F cold cup biopsy forceps to obtain tissue may be followed by holmium:YAG ablation.<sup>109</sup> Vascular lesions (arteriovenous malformations or hemangiomas) are better treated with lasers with coagulative effects greater than holmium:YAG, such as Nd:YAG or KTP. Nonetheless, successful treatment of renal bleeding using the holmium:YAG laser at 0.5 J and 5 Hz has been described in 4 patients.<sup>110</sup>

Because holmium:YAG has a predominant ablative effect, patients with bleeding diatheses may tolerate holmium:YAG ablation of upper tract transitional cell carcinoma quite well. In the series by Kuo et al, one patient with an upper pole tumor was successfully treated with holmium:YAG ablation while still on warfarin. The patient did not have a drop in hematocrit, but did have oliguria secondary to a ureteral blood clot, which was treated with a furosemide-induced diuresis.<sup>42</sup> Another advantage of holmium:YAG's ablative effect with little coagulation is that there is less risk of ureteral stricture after holmium:YAG ablation of upper tract tumors compared to electrocoagulation.<sup>111</sup>

The holmium:YAG laser is useful for management of retained ureteral stents with large stone burdens in the bladder and kidney.<sup>112</sup> In this setting, the bladder stone is treated cystoscopically with holmium:YAG irradiation. Once it is cleared of stone, the stent may be divided close to the ureteral orifice, using either holmium:YAG irradiation or endoscopic scissors. This maneuver facilitates subsequent removal of the remaining stent through a percutaneous nephroscopy access. The distal portion of stent is removed. The bladder stone debris is irrigated from the bladder. The patient is positioned prone and the remaining stent and renal stone burden adherent to the stent are managed through a percutaneous nephrolithotomy.

The holmium:YAG laser will easily incise metal and most suture materials.<sup>9,113</sup> Although rarely indicated, we have used the holmium:YAG laser to incise an impacted stone basket after it had engaged a calculus, in order to free the stone and withdraw the basket. The laser may also be used for retained intraluminal sutures that cause stones or infection. The holmium:YAG laser has also been used successfully for retrograde ureteronephroscopic incision of a renal infundibular stenosis, and thus avoiding the morbidity of a percutaneous or open approach.<sup>114</sup> Rarely, the urologist is asked by a general surgery colleague to assist in the endoscopic management of biliary calculi, and the holmium:YAG laser may be useful here.<sup>115–117</sup> We have used the laser successfully for 2 common bile duct calculi, through a percutaneous T-tube tract.

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## Laparoscopic radical nephrectomy

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### Pathological aspects of renal cell carcinoma

#### *Incidence and etiology*

Renal cell carcinoma accounts for 3% of all adult malignancies. Annual incidence in the industrialized countries is reported at between 9 and 11 per 100,000 inhabitants,<sup>1</sup> whereas the global figures show an incidence of 2.4–4.3 cases per 100,000 inhabitants.<sup>2</sup> At the time of diagnosis, 20% of the patients have disseminated disease and another 25% will have locally advanced tumors.<sup>3</sup> Around 60% of the patients who are clinically diagnosed will die due to the disease because of progression and metastatic spread.<sup>4</sup>

Renal cell cancer occurs primarily in the 5th to 6th decade. Men are twice as often afflicted as women. There is some evidence that renal cell carcinoma is more common in the urban population, due to the exposition to carcinogenic industrial agents and tobacco abuse.

Renal cell carcinoma is the most common renal tumor, accounting for 85% of all renal malignancies. The origin of the tumor is reported by a number of investigations<sup>5–7</sup> as being mainly from the proximal tubular cells (clear cell and chromophile carcinoma), followed by the distal tubular system (chromophobe carcinoma), and the collecting system (Bellini duct carcinoma).

The identification of specific genetic alterations has led to the classification of different genetic subtypes beyond the morphology of the cells, such as that described by Kovacs et al.<sup>8</sup> The main interest in this classification is that different genetic subtypes (Table 34.1) have significant different clinical behaviors as regards the course of the disease and the response to therapy. Conventional renal cell carcinomas have a poorer prognosis than papillary renal cell carcinoma.<sup>9,10</sup> Patients with chromophobe renal cell carcinoma survive longer and have less advanced disease than patients with conventional or papillary renal cell carcinoma.<sup>11,12</sup> Tumor progression and more malignant behavior has been associated with various genetic and subtype specific alterations such as duplication of chromosome 5q22 for conventional renal cell carcinoma and trisomy of chromosome 3/3q or loss of chromosome Xp in papillary renal cell types. DNA flow cytometry data also suggest that both prognosis and tumor progression rate may correlate with nondiploid tumor patterns in all subtypes.<sup>13–15</sup> The knowledge of these genetic variabilities is an important step in understanding the different responses of renal cell carcinoma to immunotherapy or other treatment modalities.

**Table 34.1** *Heidelberg classification of renal cell carcinoma*

| Subtypes of renal cell carcinoma (incidence)            | Genetic alterations   |
|---|---|
| Conventional renal cell carcinoma (clear cell) (75–80%) | Allelic loss of chromosomes 3p, 6q, 8p, 9p, 14q; duplication of 5q; mutation in VHL gene                  |
| Papillary renal cell carcinoma (10–15%)                 | Trisomies of chromosomes 3q, 7, 8p, 12q, 16q, 17q, 20; loss of Y chromosome in male                       |
| Chromophobe renal cell carcinoma (1–3%)                 | Monosomy of chromosomes 1, 2, 6, 10, 13, 17, 21   |
| Bellini duct carcinoma (1–2%)                           | No specific alterations established; loss of DNA sequences in chromosomes 1, 2, 9, 11 and 18 is discussed |
| Nonclassified renal cell carcinoma (3–5%)               | No specific alterations established   |

*Pathologic factors*

The TNM (tumor-node-metastasis) classification of the UICC (The International Union against Cancer) is today the worldwide established clinical staging system that demonstrates the anatomic extent of the malignancy; it has taken over from other classification systems (i.e. Robson stage I–IV). The TNM classification takes into account tumor size, invasion beyond the Gerota's fascia, local spread into veins, lymph node and/or adrenal metastasis, and distant metastasis (Table 34.2). All these factors are significant in predicting the clinical outcome of the disease. Patients with tumors limited to the kidney have 85–95% 5-year survival rates, whereas those with distant metastases have a poor prognosis with a 5-year survival rate of <5%.<sup>16–20</sup> In organ-confined renal cell carcinoma, the microscopic invasion of the renal vein significantly influences the course of the disease, with a poorer 5-year survival rate of 77%.<sup>16</sup> Patients with tumor invasion of the perirenal fat or Gerota's fascia have worse prognosis, with about 50% 5-year survival compared to those with organconfined disease.

The importance of renal vein invasion as an independent predictor of prognosis is controversially discussed in the literature; the frequency is reported at between 5 and 36%.<sup>21,22</sup> There is some evidence that renal vein invasion alone does not adversely affect survival when the tumor is organ-confined.<sup>23</sup> Similarly, the involvement of the vena cava inferior has no significant impact on survival; 5-year survival rates of 47–69% were published for both

**Table 34.2** *TNM classification of renal cell carcinoma (UICC 1997)*

| Stage | Description   |
|-------|---|
| T1    | Tumor limited to the kidney, 7 cm or less in diameter   |
| T2    | Tumor limited to the kidney, more than 7 cm in diameter |
| T3a   | Invasion of the adrenal gland or perirenal fat          |
| T3b   | Invasion of renal vein or infradiaphragmal vena cava    |
| T3c   | Invasion of supradiaphragmal vena cava                  |

|    |   |
|----|---|
| T4 | Tumor infiltration beyond Gerota's fascia |
| N1 | One lymph node metastasis                 |
| N2 | More than one lymph node metastasis       |
| M1 | Distant metastasis                        |

patterns.<sup>24,25</sup> Therefore, an aggressive surgical approach is accepted in cases of vein invasion.

Lymph node involvement implicates a survival rate from 5 to 30% at 5 years.<sup>23</sup> Johnsen and Hellsten reported from autopsy studies that all cases with lymphatic spread also had distant metastases.<sup>26</sup> Therefore, the benefit from an extensive lymphadenectomy is controversial. Incidental detection of unsuspected lymph node metastasis has been reported only in the range of 3%.<sup>27</sup>

Similarly, patients with adrenal gland metastasis also have distant or lymph node metastases, so that only 0.5–2% of them benefit from an adrenalectomy.<sup>28</sup> Some authors therefore recommend that ipsilateral adrenalectomy should only be performed if a lesion is detected preoperatively on a computed tomography (CT) scan or if the renal cell carcinoma is located at the upper pole region of the kidney.<sup>29</sup>

Studies of patients with metastatic disease have shown a prognosis with 5-year survival rates of between 2 and 10%.<sup>17,30</sup> The synchronous presentation of the metastatic disease is associated with a longer survival time compared to patients with asynchronous diagnosis of metastasis; in particular, patients with resectable solitary metastasis are reported to have a 5-year survival rate of 23%.<sup>31</sup>

Apart from the pathologic stage of the tumor (TNM) a number of histopathologic grading systems with regard to cell type, necrosis rate, and nuclear shape have been established. The nuclear grade is the most important independent factor correlating with survival for all stages of renal cell carcinoma.<sup>32</sup> Nevertheless, its application in clinical practice is difficult, due to the high inter-observer variation. Techniques such as nuclear morphometry are promising more objective and reproducible results in grading renal cell carcinoma, but only a few results with this method have been published regarding its prognostic significance.<sup>33</sup>

### **Surgical treatment of renal cell carcinoma**

The reported worldwide steady increase of incidence might undoubtedly be a result of the increasing availability of ultrasonography or CT. Because more incidental renal tumors are being diagnosed, the profile of patients seeking treatment for renal carcinoma has changed. Therefore, treatment strategies with different approaches (i.e. highintensity focus ultrasound, radiofrequency ablation, cryotherapy, radical and partial surgery, laparoscopy) reflect this situation in current reports. Nevertheless, surgical removal is still considered to be the dominant procedure in the management of renal cell carcinoma. During the last 10 years, however, open surgery has increasingly been replaced by the laparoscopic approaches.

## History of laparoscopic radical nephrectomy

Clayman et al pioneered laparoscopic nephrectomy, when removing a renal oncocytoma in 1990.<sup>34</sup> Almost 1 year later Coptcoat et al used the same technique for a radical extirpation of a T2 renal cell carcinoma.<sup>35</sup> In 1992, Chiu et al reported on a laparoscopic nephroureterectomy for malignant disease.<sup>36</sup> This technique has become one of the most innovative challenges to the conventional and traditional gold standard of the open approach. Currently, this option is preferred over surgery in many uro-oncologic centers all over the world, particularly focused towards T1 tumors.<sup>37</sup>

Numerous experiences worldwide have demonstrated very good surgical results and low perioperative morbidity, at least comparable to or better in many aspects than open surgery.<sup>38</sup> Additionally, a few published series with longterm follow-up now show a similar oncologic result to the open counterpart.<sup>38</sup> The technique, however, is still demanding, as it requires adequate skills in laparoscopic surgery. The further refinement of the laparoscopic technique is accompanied by a growing number of urologists being adequately trained in this area.

The basic oncologic surgical principles applied to laparoscopic surgery are exactly the same as for open surgery. Moreover, the criteria used for diagnosis, staging, follow-up, and general management are identical as well. Thus, the objective of this chapter is to focus more on the technical aspects of the procedure rather than on those aspects of the disease. Additionally, we review the current state of the art of laparoscopic radical nephrectomy, including a review of long-term follow-up data based on own experience and on the literature.

## Technique of laparoscopic radical nephrectomy

Principally, there are two approaches for laparoscopic radical nephrectomy: the transperitoneal and retroperitoneal technique.

### *Transperitoneal approach*

#### **Patient preparation**

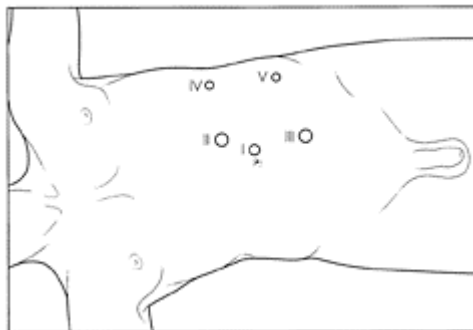
All patients receive similar preoperative preparation as performed prior to open surgery (including informed consent and bowel preparation). Prior to the procedure, a nasogastric tube and a urinary catheter are inserted. Under general anesthesia, the patient is placed in the lateral traditional flank position, with the table flexed to extend the uppermost flank; the table is then turned to a more oblique position (Figure 34.1).

### Trocar placement

After a pneumoperitoneum is attained with the inserted Veress needle, placed lateral to the rectus abdominis muscle on the line with the umbilicus, trocars are inserted through the ventral abdominal wall. Port I (10 mm) is located periumbilically at the lateral edge of the rectus abdominis muscle; Port II (5 mm for the left, 12 mm for the right side) is located subcostally on the mammillary line. Port III (12 mm for the left, 5 mm for the right side) is located above the superior iliac spine on the mammillary line (see Figure 34.1). The laparoscope is passed through Port I and used for endoscopic control of secondary trocar insertion. The ports are fixed with a sterile adhesive tape and sutured to the skin (no grips preferred). After complete inspection of the abdomen, either the descending (left kidney) or ascending (right kidney) colon is mobilized through a laterocolic incision of the peritoneum along the line of Toldt. Since the respective colon is free to fall off medially (Figure 34.2), one or two further 5 mm ports can be inserted through the newly exposed retroperitoneum (Ports IV, V). These two ports are mainly used to grasp the kidney during dissection and for kidney retrieval.<sup>37,39</sup>

### Clipping the ureter

The gonadal vein is identified in proximity to the sacral promontory, and clipped and dissected, as is the ureter

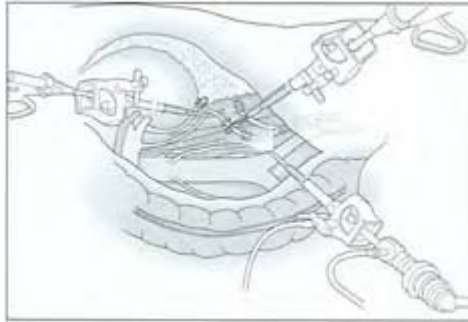


**Figure 34.1** Transperitoneal laparoscopic radical nephrectomy—patient positioning and trocar placement for left renal tumor. Positions of ports I–V are indicated.

thereafter (Figures 34.2 and 34.3). Retraction of the ureter can be established with an ENDO BOWEL clamp inserted through Port IV or V and may be helpful during dissection of the renal hilum. The lower pole of the kidney is isolated, including the fatty capsule.

### Renal vessel control

Once the vessels are identified and dissected, the clipping and transection is performed, following the principles of open surgery and starting with the artery. There are a number of different ligating systems, including the LaproClip® (Tyco-Braun), an absorbable single ligating clip; the Challenger® titanium clip (Aesculap); the nonabsorbable lockable plastic Hemo-lock-clips® (Weck); or the EndoGIA® endoscopic stapling device (Tyco), particularly used for the vein. On most occasions, we prefer titanium clips for the artery (three clips on the stay side) and the



**Figure 34.2** Transperitoneal laparoscopic radical nephrectomy-dissection and clipping of the ureter.



**Figure 34.3** Transperitoneal laparoscopic radical nephrectomy-dissection and clipping of the ureter (endoscopic view).

Lapro-Clip for the renal vein. Only for larger renal veins, do we prefer an endoscopic stapler (Figure 34.4). Dissection of the renal vessels is carried out bimanually with EndoShears, endodissector, and right-angle-clamp, quite similar to open surgery.

### Organ retrieval

Now the upper pole of the kidney, including the fatty capsule, is dissected free of the respective adrenal gland and the relevant peritoneum. Next, the organ is grasped in the hilar region and moved down into the pelvic area, preventing any interference with insertion of the organ bag. In selected cases (i.e. upper pole renal cell carcinoma) we have additionally taken out the adrenal gland by use of clips or the Endo-GIA stapler. For retrieval of the specimen we strongly recommend the LapSac, because of the strength and rigidity of the organ bag, particularly when further morcellation of the specimen is planned (Figure 34.5). The LapSac is twirled around a 4.5 mm converted reduced Endo Grasp and passed through Port III. The organ bag unfolds intra-abdominally and is held open by three Endoclamps (via Port II, IV, and V) while the kidney is maneuvered into the LapSac.<sup>40</sup>

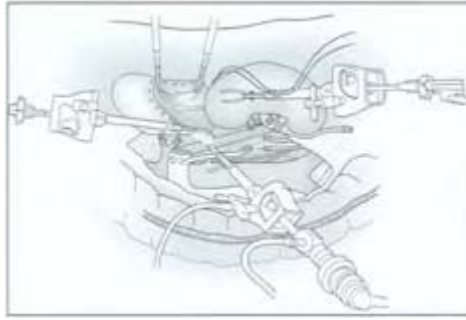
### Digital fragmentation

After the endodissector pulls the drawstring, thereby closing the bag, the trocar sleeve is removed and the neck of the bag is pulled out over the surface of the abdomen (via Port II for the right kidney and Port III for the left side). The port site is further incised (20 mm) and covered



**Figure 34.4** Transperitoneal laparoscopic radical nephrectomy-clipping and transsection of a large renal vein with the endoscopic stapler (Endo-GIA, Tyco).





**Figure 34.5** Transperitoneal laparoscopic radical nephrectomy—Entrapment of the specimen in the organ bag (LapSac).



**Figure 34.6** Transperitoneal laparoscopic radical nephrectomy—digital fragmentation and stepwise removal of specimen with ring forceps.

with an adhesive drape, making forceps removal of fatty tissue and digital fragmentation of the kidney into 3–5 pieces possible (Figure 34.6). This is done very carefully to distinguish between fatty capsule, normal renal tissue, and renal tumor, which is sent separately for histopathologic analysis. We never used a mechanical liquidizer, aspirator, or morcellator device.<sup>34,41</sup>

### Complete organ removal

In some cases we have used a 8–10 cm muscle-splitting lower abdominal incision for complete organ removal.<sup>42,43</sup> This access can also be used for a *hand-assisted laparoscopic*



**Figure 34.7** Transperitoneal laparoscopic radical nephrectomy—removal of the complete specimen via a muscle-splitting incision in the lower abdomen. This incision can also be used for a handassisted technique.

*approach*, particularly towards the end of the procedure (Figure 34.7).

Before all trocar sleeves are removed under direct vision, the renal fossa has to be inspected to rule out any active bleeding. This permits drainage of blood and irrigation fluid and may reveal postoperative bleeding. The enlarged incision (for organ removal) is closed with fascia and skin suture. All other port incisions are sutured sub- and intracutaneously or covered with adhesive strips.

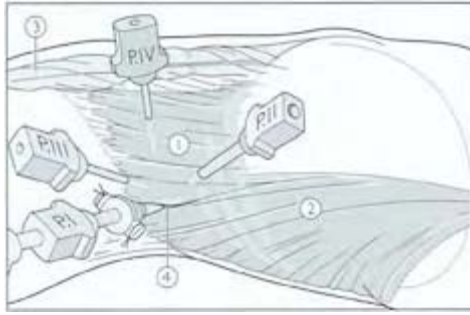
### *Retroperitoneal approach*

#### **Patient preparation**

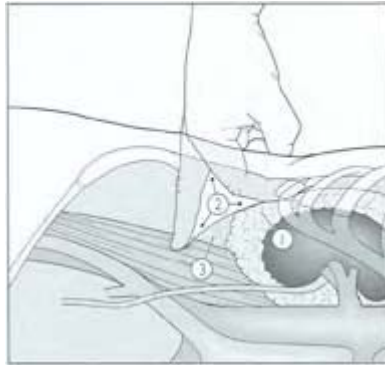
All patients receive similar preoperative preparation as performed prior to open surgery or transperitoneal laparoscopic nephrectomy.

#### **Access to the retroperitoneum**

Under general anesthesia, the patient is placed in the typical kidney position. The Trendelenburg position is not necessary. A 15–18 mm incision is made in the ‘musclefree’ triangle between the lateral edges of the M. latissimus dorsi and M. obliquus externus (Figure 34.8). A canal down to the retroperitoneal space is then created by blunt dissection with Overhold forceps. The canal is then dilated with the index finger, which dissects the plane between the lumbodorsal aponeurosis and Gerota’s fascia, pushing the peritoneum medially, and thus creating a retroperitoneal cavity for correct placement of the secondary trocars (Figure 34.9).



**Figure 34.8** Retroperitoneal laparoscopic radical nephrectomy-patient positioning and trocar placement. 1=M. obliquus externus, 2=M. latissimus dorsi, 3=M. rectus abdominis, 4=musclefree triangle. Positions of Ports P.I-P.IV are indicated.



**Figure 34.9** Retroperitoneal laparoscopic radical nephrectomy-finger dissection of the retroperitoneal space between the lumbodorsal aponeurosis and Gerota's fascia. 1=perirenal fat, 2=retroperitoneal space, 3=Gerota's fascia.

### Placement of secondary trocars

We then place the next two secondary trocars directly under palpation lateral to the index finger introduced via the primary access.<sup>44</sup> To avoid any injury to the surgeon's finger, the canal needs to be dilated using forceps (Figure 34.10): Port II (10/11 mm) for the right hand of the surgeon (use of EndoShears and Endoclip applicator); Port III (5 mm) for the left hand of the surgeon (use of endodissector). Then, the trocar site of Port I is closed with a mattress suture around the sheath to avoid gas leakage and the trocar is connected to the CO<sub>2</sub> insufflator to establish a pneumoretroperitoneum (12 mmHg, 3.5 l/min), and retroperitoneoscopy is performed.



**Figure 34.10** Retroperitoneal laparoscopic radical nephrectomy—placement of secondary trocars under palpatory control.



**Figure 34.11** Retroperitoneal laparoscopic radical nephrectomy—

dissection of the renal artery with  
right-angle forceps.

Finally, if necessary, medially to the edge of the peritoneum, another 5 mm trocar (Port IV) is inserted under endoscopic view, serving for retraction of the kidney during the dissection. As with the open procedure, the surgeon and the camera assistant stand on the dorsal side of the patient.

### **Early control of the renal artery**

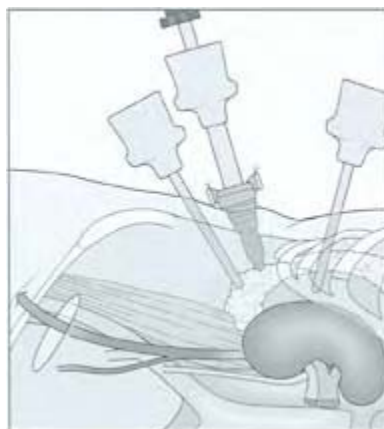
The first step in the retroperitoneal approach is the horizontal incision of Gerota's fascia to expose the psoas muscle. Thereafter, the renal hilum can be accessed easily followed by dissection of the renal artery using right-angle forceps (Figure 34.11). Subsequently, the renal artery is clipped and transected, followed by isolation of the renal vein. Early control of the renal hilum is one of the main advantages of the retroperitoneal approach.

### **Dissection of the kidney and ureter**

After early control of the hilar vessels, the lower pole of the kidney and the ureter are dissected, identifying and transecting the gonadal vein (Figure 34.12). Finally, the upper



**Figure 34.12** Retroperitoneal laparoscopic radical nephrectomy-  
dissection of the ureter and gonadal  
vein.



**Figure 34.13** Retroperitoneal laparoscopic radical nephrectomy-en bloc removal of the specimen via a muscle-splitting retroperitoneal incision in the lower abdomen.

pole and the medial part of the kidney are dissected, which includes the perirenal fat. When indicated, the adrenal gland is taken en bloc with the specimen, requiring clipping of the adrenal vessels.

### **Organ entrapment**

For adequate retrieval of the specimen, an adequate organ bag (i.e. LapSac) has to be inserted. The organ bag is pulled out on the skin surface via Port I. For morcellation of the specimen, the initial incision is enlarged to 25–30 mm. En bloc removal of the specimen can also be performed via a muscle-splitting retroperitoneal incision in the lower abdomen (Figure 34.13).

## **Heilbronn experience with laparoscopic radical nephrectomy**

### *Patients*

Since 1992, we have performed in the Department of Urology at the SLK-Klinikum in Heilbronn 80 laparoscopic radical nephrectomies in 78 patients (48 male, 30 female) with localized renal cell carcinoma. Stage and grade are listed in Table 34.3; the majority were pT1 tumors, and there had been two bilateral renal cell carcinomas in patients under dialysis. All relevant perioperative data were recorded, concerning operative time, complications, conversion, and reintervention rate, as well as hospital stay (Table 34.4). The follow-up time averaged 80 (7–144) months. Outcomes were determined by local

recurrence, regional progression, development of metastases, and disease-specific survival.

**Table 34.3** *Heilbronn experience with laparoscopic radical nephrectomy—pathological classification*

| Tumor                | Stage <i>n</i> |
|----------------------|----------------|
| Renal cell carcinoma | pT1 38         |
|                      | PT2 10         |
|                      | pT3a 3         |
|                      | pT3b 2         |
|                      |                |
| Oncocytoma           | 2              |
| Total                | 55             |

**Table 34.4** *Heilbronn experience with laparoscopic radical nephrectomy—perioperative data*

| Criteria                   | Nephrectomy (RCC) |
|----------------------------|-------------------|
| Total number               | 80                |
| Access:                    |                   |
| • Transperitoneal          | 18                |
| • Retroperitoneal          | 62                |
| Specimen retrieval:        |                   |
| • Morcellation             | 25                |
| • By incision              | 55                |
| Mean operating time        | 141 min           |
| Mean blood loss            | 135 ml            |
| Conversion to open surgery | 0                 |
| Complications:             | 5.0%              |
| • Bleeding                 | 1                 |
| • Pulmonary embolism       | 1                 |
| • Ileal stenosis           | 1                 |
| Reintervention             | 1                 |
| Hospital stay              | 7 days            |
| Back to normal activity    | 21 days           |
| RCC=renal cell carcinoma.  |                   |

## Results

### Perioperative data

The operating time averaged 141 (90–410) min; there was no difference whether a transperitoneal ( $n=18$ ) or retroperitoneal ( $n=62$ ) approach was used (see Table 34.3). In 25 cases the specimen was entrapped in an organ bag (LapSac<sup>®</sup>, Cook Urological,

Spencer, Indiana) and retrieved after digital morcellation, whereas in 55 instances the intact organ was removed via a 6–8 cm incision in the lower abdomen (see Figures 34.7 and 34.13). In 5 cases, this incision was also used for manual assistance during the procedure. The mean estimated blood loss was 135 (100–700) ml. There was no conversion to open surgery.

We observed one bleeding from the surface of the spleen, which could be managed by laparoscopic tamponating using a hemostatic gauze (Tachotamp®, Ethicon, Norderstedt, Germany). Another patient developed bleeding from one of the trocar sites (Port III) 6 hours after a right radical nephrectomy, which was controlled by a transcutaneous suture. Two months later the same patient suffered from ileus due to a stenosis of the terminal ileum, most probably induced by the aforementioned suture. The patient was successfully treated by a segmental ileal resection. One patient had a pulmonary embolism which could be managed conservatively. The mean postoperative hospital stay was 7 (4–16) days (see Table 34.4).

### Pathology

The tumor was right sided in 33 (41%) patients, left sided in 43 (54%), and bilateral in 2 (5%) patients. The tumor was located at the upper pole in 21 (26%), at the central area in 40 (50%), and at the lower pole in 19 (24%) of the cases. Mean tumor size was 4.1 cm (range 0.5–8). The pathologic examination revealed renal cell carcinoma in 78 (97.5%) and an oncocytoma in 2 (2.5%) specimens. In the renal cell carcinoma group, the tumor stage was pT1 in 61 (76%), pT2 in 12 (15%), pT3a in 3 (45%) and pT3b in 2 (2.5%) of the specimens. Since we did not use any morcellator (i.e. Cook morcellator), the pathologist was able to define the exact pathologic staging in all cases. The surgical margins were negative in all cases.

### Follow-up data

The mean observation time was 65 months (36–85 months). There was no port-site metastasis. One patient with a pT2G2 tumor developed a local recurrence and bone metastases 4 years after laparoscopic radical nephrectomy. He died 56 months after the procedure. Another 3 patients with pT1G3, pT2G3 and T3a tumor developed pulmonary and bony metastases 12, 18 and 31 months after the procedure and died 34 months after surgery. The cumulative overall disease-free survival rate after 5 years is 91%, revealing 96% for pT1/pT2 and 82% for pT3 tumors (Table 34.5).

**Table 34.5** *Heilbronn experience with laparoscopic radical nephrectomy—follow-up data*

| Criteria                        | Radical nephrectomy (RCC) |
|---------------------------------|---------------------------|
| Total                           | 55                        |
| Mean observation time           | 65 months                 |
| Dead of disease                 | 4                         |
| Dead of other causes            | –                         |
| Overall survival                | 91%                       |
| Disease-free survival (5 years) |                           |



- Overall 91%
  - pT1/pT2 96%
  - pT3 80%
- RCC=renal cell carcinoma.

### Worldwide experience with laparoscopic radical nephrectomy

Laparoscopic radical nephrectomy has largely overtaken traditional surgery in many centers all over the world (Table 34.6). Beyond the discussion of access (retroperitoneal or transperitoneal), the contemporary review of the literature documents the perioperative benefits of laparoscopy compared to the open approach.

In a multicenter study, Ono et al<sup>45</sup> compared 103 patients operated on by laparoscopy (85 transperitoneal and 18 retroperitoneal) with 46 operated on by the classic open procedure. The mean blood loss was documented as 254 ml vs 465 ml and the mean of the patients requiring transfusion were 5% vs 9% respectively for the two groups (see Table 34.6).

Gill et al<sup>46</sup> compared, retrospectively, 34 patients operated on laparoscopically using a retroperitoneal approach with 34 patients who underwent traditional open methods. They found a mean blood loss of 97.4 ml vs 295.1 ml and a complication rate of 13% vs 24% for comparable cases (see Table 34.6).

The meta-analysis of minor complications is reported in the current literature between 3 and 15% and major complications between 3 and 10% (Table 34.7). In open cases a complication rate between 10 and 20% was described for similar tumor stages.<sup>47</sup> The complication rate of 34% published by Dunn et al<sup>48</sup> rather reflects the learning curve of the pioneer and the benefit other centers gained from this experience.

**Table 34.6** *Laparoscopic vs open radical nephrectomy—review of the literature*

| Criteria              | Abbou et al <sup>37</sup> |     | Ono et al <sup>45</sup> |     | Gill et al <sup>46</sup> |     | Jeschke et al <sup>66</sup> |      |
|-----------------------|---------------------------|-----|-------------------------|-----|--------------------------|-----|-----------------------------|------|
|                       | Lap                       | Op  | Lap                     | Op  | Lap                      | Op  | Lap                         | Op   |
| Patients ( <i>n</i> ) | 29                        | 29  | 103                     | 46  | 34                       | 34  | 31                          | 34   |
| Tumor size (cm)       | 4.1                       | 5.7 | 3.1                     | 3.3 | 5.0                      | 6.1 | 3.8                         | 5.7  |
| OR time (min)         | 145                       | 121 | 282                     | 198 | 186                      | 174 | 125                         | 145  |
| Blood loss (ml)       | 100                       | 285 | 254                     | 465 | 98                       | 370 | na                          | na   |
| Complication (%)      | 7                         | 27  | na                      | na  | 13                       | 24  | na                          | na   |
| Hospital stay (days)  | 4.8                       | 9.7 | na                      | na  | 1.4                      | 5.8 | 6.8                         | 11.5 |
| Follow-up (months)    | 15                        | 13  | 29                      | 39  | 10                       | 29  | na                          | na   |

Lap=operated on by laparoscopy, Op=operated on by the classic open procedure, OR=operating room, na=not available.

**Table 34.7** *Worldwide experience of laparoscopic radical nephrectomy—perioperative data*

| Main author              | Patients (n) | Operating time (h) | Blood loss (ml) | Complication rate |       | Conversion | Hospital stay (days) |
|--------------------------|--------------|--------------------|-----------------|-------------------|-------|------------|----------------------|
|                          |              |                    |                 | Minor             | Major |            |                      |
| Barret <sup>59</sup>     | 72           | 2.9                |                 | 3%                | 8%    | 8%         | 4.4                  |
| Abbou <sup>37</sup>      | 29           | 2.4                | 100             | 8%                |       | 3.4%       | 4.8                  |
| Dunn <sup>64</sup>       | 60           | 5.5                | 172             | 34%               | 3%    | 1.6%       | 3.4                  |
| Ono <sup>45</sup>        | 103          | 4.7                | 254             | 3%                | 10%   | 3.4%       |                      |
| Chan <sup>64</sup>       | 67           | 4.2                | 289             | 15%               |       | 1.5%       | 3.8                  |
| Gill <sup>62</sup>       | 100          | 2.8                | 212             | 11%               | 3%    | 2%         | 1.6                  |
| Janetschek <sup>58</sup> | 121          | 2.4                | 154             | 5%                | 4%    | 0%         | 6.1                  |
| Rassweiler*              | 80           | 2.5                | 135             | 5.0%              |       | 0%         | 7                    |

\* Present series.

The mean operating time, initially reported in the range of 240 min, decreased in recent publications to 150 min (see Tables 34.6 and 34.7). We made the same observation (see Table 34.4), underlining the importance of the learning curve in achieving comparable or better operating times than the open approach.<sup>46,48,49</sup> A major key to that problem is that the same experienced laparoscopic team treats all cases. Dunn et al reported a decrease of the operating time by nearly half comparing the first 10 and the last 10 patients who underwent a laparoscopic radical nephrectomy in the same institution.<sup>48</sup>

As far as the duration of the hospital stay was concerned, different authors described a significant advantage of laparoscopy: Gill et al<sup>46</sup> 1.4 vs 5.8 days; Abbou et al<sup>37</sup> 4.8 vs 9.7 days.

The comparison of complication rate, length of hospital stay, blood loss, and a decreasing operating time confirms significant lower perioperative morbidity (see Table 34.7). Much more important than the technical feasibility of laparoscopic radical nephrectomy is the long-term outcome. In the meantime, studies are available with longer follow-up, including our own experience (Table 34.8). It has to be noted that, at the beginning all authors limited their range of indications to small-sized renal tumors (3–6 cm) according to clinical stage T1. However, like in our series, histopathology also evidenced pT3 tumors among the treated cases.<sup>50–52</sup> This has to be taken into consideration when looking at the long-term results. The overall 5-year disease-free survival rates are excellent, ranging between 89 and 96% (see Table 34.8). Portis et al recently published the long-term follow-up of a multi institutional study with a mean follow-up of 5 years. The authors observed equivalent overall survival (81 vs 89%), cancer-specific survival (98 vs 92%), as well as recurrence-free survival (92 vs 92%) rates compared to the traditional open technique in these centers.<sup>38</sup> Our own 5-year experience at Heilbronn confirms these results (see Tables 34.5 and 34.8).

## Discussion

Since the first laparoscopic nephrectomy reported by Clayman et al in 1991,<sup>34</sup> experience with laparoscopy in urology, especially in laparoscopic nephrectomy, has increased continuously. The role of laparoscopic radical nephrectomy for malignancies of the kidney and ureter is still under debate. Primary concerns are focused on the safety of the procedure, the reproducibility of the technique compared with open surgery, and the risk of tumor cell spillage leading to port-site metastases. Further concerns have been related to cost-effectiveness and the steep learning curve of the procedure.

In the meantime, more than 10 years after one of the authors had the honor of assisting Malcolm Coptcoat with the first radical nephrectomy for renal cell cancer,<sup>35</sup> the technique of transperitoneal laparoscopic radical nephrectomy has been standardized, fulfilling all principles of urooncological surgery. During the last decade, various authors, including ourselves, have proposed a retroperitoneal approach (Tables 34.7 and 34.8), advocating the

**Table 34.8** *Worldwide experience with radical nephrectomy—oncologic aspects*

| Main author              | Patient (n) | Specimen removal       | pT stage | Surgical margin | Follow-up months | Recurrence port site/local/distant (%) | 5 -year survival |
|--------------------------|-------------|------------------------|----------|-----------------|------------------|--|------------------|
| Janetschek <sup>49</sup> | 73          | Intact                 | T1–T3a   | Negative        | 13.3             | 0/0/0                                  | na               |
| Abbou <sup>63</sup>      | 41          | Intact                 | T1–T3b   | Negative        | 24.7             | 0/2/0                                  | na               |
| Ono <sup>45</sup>        | 103         | Morcellated and intact | –        | –               | 29               | 0/1/3                                  | 92%              |
| Chan <sup>64</sup>       | 67          | Morcellated and intact | T1–T3b   | Negative        | 35.7             | 0/0/3                                  | na               |
| Gill <sup>65</sup>       | 100         | Intact                 | T1–T3b   | Negative        | 16.1             | 0/0/2                                  | na               |
| Portis <sup>38</sup>     | 64          | Morcellated and intact | T1–T3b   | Negative        | 54               | 0/1/2                                  |                  |
| Rassweiler*              | 80          | Morcellated and intact | T1–T3b   | Negative        | 65               | 0/2/4                                  | 91%              |

na=not applicable; \*=present series.

advantage of earlier control of the renal artery and the reduced need for dissection (i.e. deflection of the colon). However, we feel that, like in open surgery, the access should be of secondary interest. The reproducibility of the procedure has been documented in multicenter studies,<sup>46,47</sup> as well as in a review of the literature. The complication rate is acceptable and still decreasing; with increasing experience, even the operative time does not exceed that of open surgery (see Tables 34.3, 34.6, and 34.7). The retrieval of the

specimen is accomplished mostly by a small incision after entrapment in an organ bag rather than by morcellation.

Some authors have used this incision earlier during the procedure to perform hand-assisted laparoscopy (see Figure 34.7). They emphasize that this would speed up the procedure and reduce the learning curve.<sup>39,42,43,48</sup> According to our own early experience, we could reduce the operative time by about 60 min.<sup>42,43</sup> However, standardization of the use of the hand has proved to be very difficult, particularly because the surgeon has to insert different hands for left- and right-sided radical nephrectomies. Particularly, with regards to a standard training program of laparoscopy and retroperitoneoscopy in urology, we feel that hand-assistance should be limited to managing problematic situations. By contrast, the increasing expertise of first-generation laparoscopists has offered a variety of dissecting techniques and retraction standards for the following generations. This enables them to perform the operations much easier and with less complications than the pioneers.<sup>53,44</sup> Subsequently our own operating room times have dropped significantly, and are now in the same range as for open surgery (see Tables 34.4 and 34.7).

Concerning the cost-benefit analysis of laparoscopic radical nephrectomy, the situation in the United States differs significantly from that in Europe: the operating times reported by the different groups are mostly longer, the charges for the operating room are higher, and the postoperative hospital stay is shorter for both open and laparoscopic surgery than in Europe.<sup>39,50,52</sup> Therefore, the higher perioperative costs of laparoscopy cannot be completely compensated by the reduction of hospital stay. At our center, we have exchanged almost all of our disposable instruments by reusable armamentarium (i.e. metaltrocars, endo-shears, endo-graspers, clip-appliers). Even if the operating time in some centers may still be 60 min longer for laparoscopy, these costs can mostly be compensated by the reduced postoperative hospital stay. Consequently, a significant benefit for the social security system can be obtained by the shorter convalescence of about 2–3 weeks compared with open surgery.<sup>50,52,55</sup>

In summary, despite some technical modifications by the different groups, laparoscopic radical nephrectomy can be regarded as a standardized and safe procedure that allows the transmission and reproduction of the surgical principles of the open procedure. Additionally, the perioperative morbidity of the patients can be reduced significantly by use of laparoscopy.

Much more important, however, is the long-term oncologic outcome of the procedure. The overall 5-year diseasefree survival rates are excellent, ranging between 89 and 96%, and do not differ from contemporary series of open surgery (see Table 34.6). Additionally, the recently published comparative study with long-term follow-up by Portis et al<sup>38</sup> was able to document almost identical results for laparoscopic and open surgery.

Even after open surgery of clinical T1 tumors, local recurrence as well as distant metastases have been observed.<sup>47,56–58</sup> It must be mentioned that, until now, among more than 2000 reported cases of laparoscopic radical nephrectomy, 3 port-site metastases have been documented.<sup>59,60</sup> However, 2 of them occurred at the same institution during the first 20 cases.<sup>68</sup> In all cases, the specimen was morcellated. Thus, the role of intact specimen removal is still controversial, although there is no difference in morbidity and oncologic outcome as reported recently.<sup>61</sup> Despite the risk of understaging the tumor on a

preoperative CT scan, morcellation can be safely performed without compromising survival.<sup>62</sup> According to our own experience, with fragmentation rather than complete morcellation of the kidney, adequate tumor staging had never been a problem.

In conclusion, despite some technical modifications concerning access, laparoscopic radical nephrectomy has become a well standardized and thus reproducible, but technically demanding procedure. Laparoscopic radical nephrectomy has met all oncologic standards in comparison to open surgery. Ideal indications are for small tumors (T1) that are not candidates for nephron-sparing surgery. The complication rates are acceptable and still decreasing. The long-term results are excellent and correspond to the results of open surgery.

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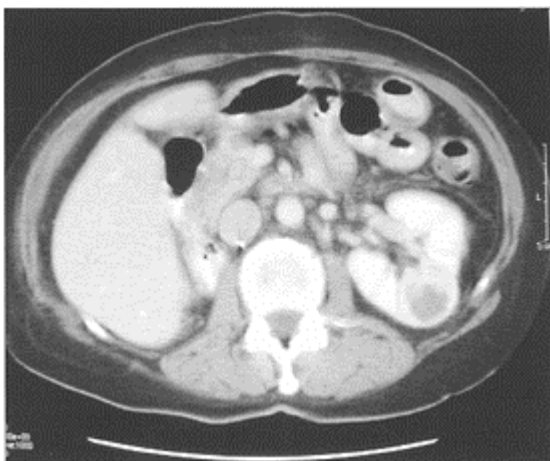
## Minimally invasive, nephron-sparing interventions for renal lesions: laparoscopy and ablative techniques\*

Yair Lotan, Jeffrey A Cadeddu, and Jay T Bishoff

### Introduction

The increase in incidentally found small renal tumors has served as an impetus to develop less-invasive parenchymalsparing techniques for tumor treatment<sup>1</sup> (Figure 35.1). Recent studies have shown that renal parenchymal-sparing procedures yield comparable outcomes with regard to tumor control compared with radical nephrectomy for small tumors.<sup>2-5</sup> The indications for partial nephrectomy include resection of nonfunctioning moieties of duplicated systems, urolithiasis in calyceal diverticula, and excision of small tumors or tumors in solitary kidneys. To reduce the morbidity of partial nephrectomy, newer minimally invasive approaches have been developed: laparoscopic partial nephrectomy (LPN) and ablative technologies. While laparoscopic techniques aim to reproduce open tumor resection with negative margins, ablative techniques aim to destroy renal tumors without the need for resection. In this chapter, we will explore the current experience with laparoscopic partial nephrectomy with a focus on the various hemostatic modalities. We will also discuss the current ablative techniques and possible future areas of development.

\* The views expressed in this article are those of the authors and do not reflect the official policy of the Department of Defense, or other Departments of the U.S. Government.



**Figure 35.1** X-ray. A 3 cm left renal lesion consistent with renal cell carcinoma. (Courtesy of Tung Shu.)

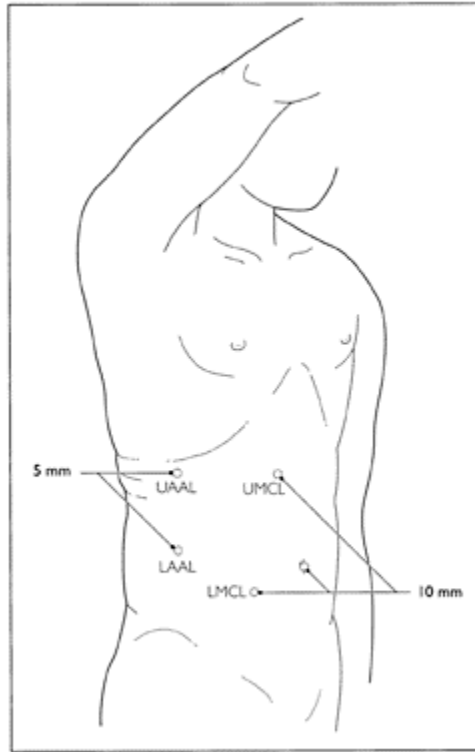
### **Laparoscopic partial nephrectomy**

With the emergence of laparoscopy as a less-morbid approach to various urologic procedures, efforts have been made to apply this technique to small renal tumors.

#### *Technical aspects*

The goal of LPN is to successfully reproduce the oncologic surgical principles of open partial nephrectomy, which include:

1. complete survey of the renal unit to exclude the presence of synchronous lesions missed by preoperative imaging



**Figure 35.2** Transperitoneal access for laparoscopic nephron-sparing renal surgery. Five trocars are used with three 12 mm trocars: one umbilicus and two mid-clavicular with upper (UMCL) and lower (LMCL) trocars and two 5 mm trocars: one in the anterior axillary line upper (UAAL) and lower (LAAL).

2. wide, en bloc tumor excision with a normal
3. vascular control and hemostasis parenchymal margin and without tumor spillage
4. water-tight closure of the collecting system

### Approach

Both transperitoneal and retroperitoneal approaches have been used for LPN (see Table 35.1). While some authors have used the transperitoneal approach exclusively<sup>6</sup> (Figure 35.2), because of its larger working space, several authors have used a retroperitoneal



|      |                               |    |  |         |  |               |       |     |        |        |   |
|------|-------------------------------|----|--|---------|--|---------------|-------|-----|--------|--------|---|
| 2002 | Gill et al <sup>8</sup>       | 50 | Transperitoneal (28)<br>Retroperitoneal (22) | Yes     | Suture over bolsters   | 270 (40–1500) | 180   | 2.2 | 1 (2)  | 6 (12) | 0 |
| 2000 | Janetschek et al <sup>9</sup> | 25 | Transperitoneal (15)<br>Retroperitoneal (10) | No      | Bipolar, argon beam, fibrin glue                                 | 287 (20–800)  | 163.5 | 5.8 | 2 (4)  | 3 (12) | 0 |
| 2001 | Stifelman et al <sup>11</sup> | 11 | Transperitoneal                              | No      | Hand assistance, harmonic scalpel, argon beam, Surgicel          | 319           | 274   | 3.3 | 0      | 2 (18) | 1 |
| 2000 | Harmon et al <sup>10</sup>    | 15 | Transperitoneal (7)<br>Retroperitoneal (8)   | No      | Laparoscopic coagulating shears, argon beam, Surgicel            | 368 (75–1000) | 170   | 2.6 | 0      | 0      | 0 |
| 2001 | Gettman et al <sup>34</sup>   | 10 | Transperitoneal (9)<br>Retroperitoneal (1)   | No      | Radiofrequency ablation  | 198 (50–700)  | 193   | NA  | 0      | 0      | 0 |
| 2001 | Yoshimura et al <sup>14</sup> | 6  | Transperitoneal                              | No      | Microwave tissue coagulator                                      | <50           | 186   | NA  | 0      | 2 (33) | 0 |
| 1999 | Hoznek et al <sup>7</sup>     | 7  | Retroperitoneal                              | Yes (5) | Bipolar, harmonic scalpel, glue                                  | 129(0–400)    | 133   | 7.3 | 1 (14) | 1 (14) | 0 |
| 2000 | Wolf et al <sup>6</sup>       | 10 | Transperitoneal                              | No      | Hand assistance (8), argon beam, gelatin sponge with fibrin glue | 460           | 199   | 2   | 0      | 3 (30) | 0 |

EBL=estimated blood loss, OR=operating room, NA=not available.



**Figure 35.4** Laparoscopic ultrasound probe (B-K Medical, Copenhagen, Denmark). Laparoscopic flexible tipped ultrasound probe is used to image renal lesions to guide for nephron-sparing therapy.

tumor(s) position relative to the collecting system and renal vasculature. Endoscopic retrieval devices like the Endocatch bag allow removal of the tumor specimen without tumor spillage, peritoneal implantation, or trocar site seeding.

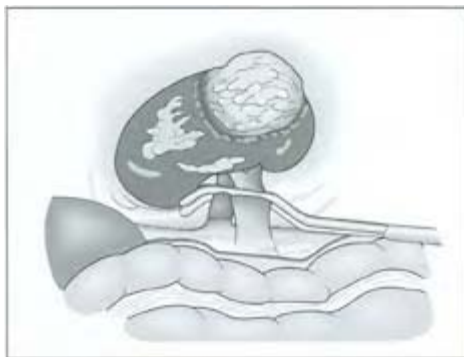
### Hemostasis

The main challenge that has limited the widespread use of laparoscopy in the management of small renal tumors has been unreliable parenchymal hemostasis. While Gill et al achieved good results with duplication of open techniques,<sup>8</sup> the difficulty of suturing and concerns with warm ischemia have led to the development of innovative means of achieving hemostasis without the need for hilar control or suturing. These techniques to decrease blood loss have ranged from the use of various energy sources, such as bipolar electrocautery,<sup>9</sup> ultrasonic scalpel,<sup>7,10,11</sup> argon beam,<sup>6,9-11</sup> laser,<sup>12,13</sup> and microwave,<sup>14</sup> to the use of tamponading devices, such as cable ties,<sup>15-18</sup> loops,<sup>19</sup> electrosurgical snare electrodes,<sup>20</sup> and hand assistance.<sup>6,11</sup> Table 35.1 provides details concerning the operative course and hemostatic control methods for various series for LPN. However, a brief discussion of each technique is warranted.

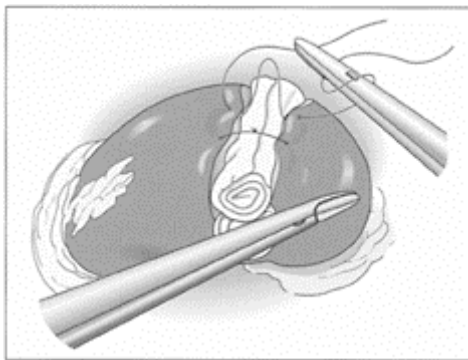
**Duplication of open techniques: suturing and hilar control.** In an effort to duplicate open surgical techniques, Gill and colleagues performed LPN in 50 patients.<sup>8</sup> Initially only the renal artery was clamped but persistent venous oozing hampered tumor excision. Subsequently, both the vein and artery were clamped using a laparoscopic Satinsky clamp with a mean warm ischemia time of 23 min (Figure 35.5). Hemostasis was achieved with intracorporeal suturing and bolsters (Figure 35.6). While this group had good results, this technique is challenging because of the advanced skills necessary to complete intracorporeal suturing in less than 30 min.

Hoznek et al also clamped the hilum for bleeding that was not controlled with bipolar coagulation. Warm ischemia never exceeded 10 min. After resection, the lesion was covered with oxidized regenerated cellulose mesh with gelatin resorcinol formaldehyde glue.<sup>7</sup>

**Hand assistance.** Hand-assisted laparoscopy has been used to decrease morbidity during radical and donor nephrectomy. Recently it has been applied to nephron-sparing surgery as well. Wolf and colleagues performed LPN in 10 patients and used the Pneumosleeve (Dexterity, Atlanta, Georgia) to facilitate this procedure in 8 patients.<sup>6</sup> The approach was transperitoneal in all cases. Use of hand assistance allowed for 'pinching' of the tumor base to tamponade bleeding. A gelatin sponge soaked with fibrin glue was applied with pressure to achieve hemostasis. In addition, the argon beam was used to seal the edges of the fibrin glue. The



**Figure 35.5** Laparoscopic partial nephrectomy. To facilitate resection of the renal tumor during laparoscopic partial nephrectomy, a laparoscopic Satinsky clamp (AESCULAP) is used to obtain control of both the renal artery and vein.



**Figure 35.6** Laparoscopic partial nephrectomy. After the resection of the renal tumor is completed, hemostasis is obtained via intracorporeal suturing of the renal parenchyma over bolsters with No. 1 polydioxanone suture.

argon beam coagulator is frequently used as a hemostatic adjunct.<sup>21</sup> There was one major complication involving an arteriovenous (AV) fistula and one of the patients who was

undergoing standard laparoscopy required conversion to hand assistance to control hemorrhage.

Stifelman and colleagues performed LPN in 11 patients, 9 of whom had <4 cm renal lesions.<sup>11</sup> They used three different devices: the Intromit (Applied Medical, Rancho Santa Margarita, California), Hand Port (Smith Nephew, Andover, Massachusetts), and Pneumosleeve. The renal artery was identified and isolated but not clamped. A combination of the harmonic scalpel and argon beam was used for resection and hemostasis. Subsequently, the intraabdominal hand was used to compress the parenchyma and Surgical (Johnson & Johnson, Summerville, New Jersey) was pressed manually into the defect. Three or four pledget sutures were then placed to reapproximate the renal capsule. The results of this technique were good with no positive margins, no transfusion requirement, and two minor complications (18%). One patient was converted to an open procedure to ensure negative margins because of deep invasion of the tumor. There were no recurrences in a mean of 8 months follow-up.

**Laser energy.** Laser partial nephrectomy has been described using the CO<sub>2</sub>,<sup>22,23</sup> Nd:YAG,<sup>12,24,25</sup> and holmium laser.<sup>13,26</sup> Lasers have different energy levels and tissue penetration according to their wavelength. The CO<sub>2</sub> laser wavelength of 10.6  $\mu$ m provides sharp cutting with minimal tissue penetration. Compared with the CO<sub>2</sub> laser, the Nd:YAG laser (1064 nm) has a deeper thermal effect and thus improved tissue coagulation. Because of the shallow tissue penetration of the CO<sub>2</sub> laser, adequate hemostasis of larger vessels is problematic even with hilar occlusion.<sup>22,23</sup> Benderev et al. performed open lower pole laser partial nephrectomy in six dogs following hilar occlusion.<sup>25</sup> While there was minimal blood loss, two large urinomas occurred, suggesting that the laser may not adequately seal the collecting system.

The holmium:YAG laser operates in the near infrared region of the electromagnetic spectrum (2100 nm) and is effective in cutting through soft tissue. Lotan et al developed a successful technique of laparoscopic Ho:YAG laser partial nephrectomy without the necessity of hilar occlusion in the porcine model and subsequently applied it successfully to 3 patients.<sup>13,26</sup> Settings of 0.2 J at 60 pulses/s provided an almost continuous delivery of energy, but higher energy of 0.8 J at 40 pulses/s was also utilized to assist with hemostasis. Importantly, with the addition of fibrin glue to the cut surface of the remaining parenchyma, the collecting system was closed. While the Ho:YAG laser provides adequate hemostasis without hilar occlusion for patients with peripheral tumors during LPN, blood splattering and smoke generation during resection can obscure the operating field and diminish its clinical value.

**Cable ties/loops.** While initial efforts using a porcine model demonstrated the potential of tourniquets for stabilization of the kidney and vascular tamponade,<sup>15</sup> the initial attempt at using a plastic tie band to control bleeding was unsuccessful in clinical practice.<sup>16</sup> Cadeddu et al later refined this technique in the laboratory<sup>18</sup> and then used it clinically.<sup>17</sup> In a porcine model, a 1-inchwide, 10-inch long standard commercial plastic cable tie was engaged in a loop and laparoscopically positioned around the lower pole, and 8 large amputations involving the collecting system and 8 smaller amputations excluding the collecting system were performed using laparoscopic scissors. Fibrin glue was applied to seal the cut surface prior to cable-tie removal. Median cable tie ischemia time was 15 min (range 7–48) and median blood loss was 30 ml (range 10–300). In each case, hemostasis was attained with fibrin glue. One animal died from urinary extravasation on



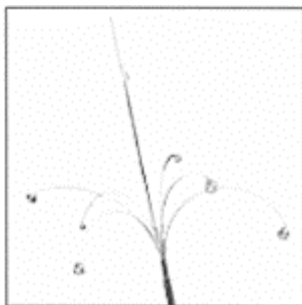
postoperative day 4. This technique was utilized in a patient with a 3 cm upper pole renal cell carcinoma.<sup>17</sup> Bleeding was kept to minimal ooze by the cable tie: estimated blood loss (EBL) <100 ml. The argon beam coagulator along with two layers of fibrin glue and oxidized cellulose, was then used to seal the parenchymal surface prior to removal of the cable tie. Two additional patients have undergone successful LPN using this technique (JA Cadeddu, pers comm).

Following a similar concept, a double-loop apparatus has also been used to stabilize the kidney and provide polar compression to allow for a retroperitoneal LPN.<sup>19</sup> The advantage of a cable tie or tourniquet technique is that it allows normal parenchyma in the remaining kidney to maintain perfusion. The obvious disadvantages are that a necessary margin of normal parenchyma between the tumor and hilum restricts the technique to polar lesions, and slippage of the cable tie off the kidney is possible.

**Endosnare.** With the aim of providing both a tourniquet effect and simultaneous hemostasis, Elashry et al have developed a unique electrosurgical snare electrode (Cook Urological Inc., Spencer, Indiana) in combination with an electrosurgical generator (ERBE USA, Inc., Marietta, Georgia) for LPN.<sup>20</sup> The endosnare device generator provides both cutting and coagulation energy. The device is positioned around the pole of the kidney and the wire is pulled through the kidney until the pole is completely transected.

This device was compared with two different ultrasonic dissectors, the Cavitron Ultrasonic Surgical Aspirator (CUSA) and the ultrasonic shears, in a porcine LPN. The electrosurgical snare was found to be significantly faster and associated with less intraoperative bleeding. However, the argon beam electrocoagulator was necessary in certain cases to control persistent oozing from the cut parenchymal surface. There was no evidence of extravasation at 6 weeks. Unfortunately, there has been no human application at this time. As with other tourniquet devices, this technique is limited to polar lesions.

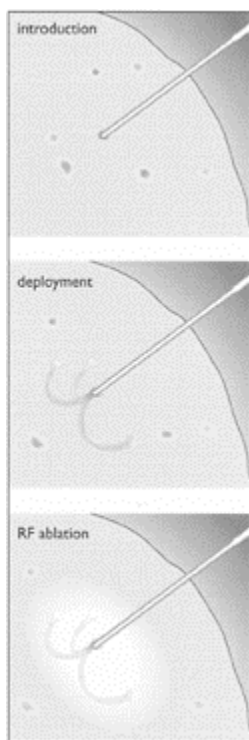
**Radiofrequency ablation assisted LPN.** While most technologic innovations focus on instruments that cut and coagulate simultaneously, radiofrequency ablation (RFA) has been used to coagulate the renal lesion prior to excision in order to prevent bleeding. Several investigators have demonstrated parenchymal thrombosis and coagulation as a result of RFA. Corwin and Cadeddu were the first to describe the use of RFA to facilitate LPN in this manner.<sup>27</sup> A 15-gauge RITA Starburst XL probe (RITA Medical Systems, Inc., Mountain View, California) was used for



**Figure 35.7** Radiofrequency ablation probe. Radiofrequency ablations of small renal lesions are carried out with a RITA Starburst XL probe (RITA Medical Systems, Inc., Mountain View, California).

RFA and was deployed approximately 0.5–1.0 cm beyond the computed tomography (CT)-measured tumor diameter (Figures 35.7 and 35.8). After ablation for 2 cycles, the tumor is resected. Experience suggests that this technique should be limited to peripheral exophytic tumors.<sup>28</sup>

**Microwave tissue coagulator.** A microwave tissue coagulator has also been used to provide hemostasis prior to resection in patients with peripheral exophytic masses.<sup>14,29–31</sup> Yoshimura et al used the Microtaze OT110M (Azwell Inc., Osaka, Japan) microwave generator with 4 probes ranging in length from 1 to 3 cm and 0.6 cm in diameter.<sup>14</sup> After laparoscopic exposure in 6 patients, the renal parenchyma was punctured with a needle-type monopolar probe along the resection line at 5–8 mm intervals. There were 5–23 coagulations performed at 70–75 W for 40–45 s per session. The tumor was subsequently



**Figure 35.8** Radiofrequency ablation. The RITA probe is placed directly into the renal lesion under ultrasound monitoring. Prongs are deployed approximately 0.5–1.0 cm beyond the measured tumor diameter to completely ablate the tumor.

resected with the endoscissors along the coagulation zone without the need for renal pedicle occlusion.

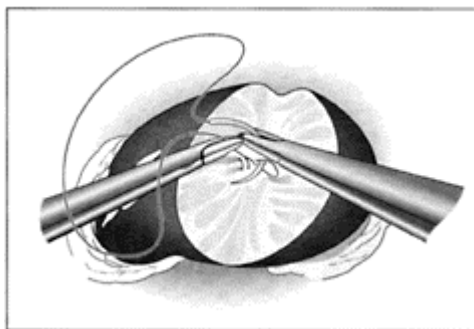
### Collecting system transection

As in open surgery, a drain should be placed after LPN to detect and drain urine leaks. Preoperative ureteral catheterization can be used to help identify calyceal injuries, and intracorporeal suture repair has been performed by some investigators<sup>8</sup> (Figure 35.9). However, materials such as oxidized cellulose mesh,<sup>10,11</sup> gelatin resorcinol formaldehyde glue,<sup>7</sup> and fibrin glue<sup>6,9</sup> have also been used successfully to seal the transected parenchyma and collecting system.

*Clinical outcomes*

Winfield et al performed the first LPN in 1992 on a patient with a lower pole diverticulum.<sup>32</sup> Subsequently, McDougall et al described their experience with 12 patients who underwent wedge resection or polar partial nephrectomy and reported a high complication rate (50%) and open conversion rate (33%) associated with LPN.<sup>33</sup>

Table 35.2 summarizes the oncologic outcomes for series of LPN. In a commendable effort to duplicate open surgical techniques, Gill and colleagues performed LPN in 50 patients.<sup>8</sup> Of these, 24 (48%) had either compromised contralateral kidney function (20) or a solitary kidney (4). The mean tumor size was 3.0 cm. The mean operative time was 3.0 hours and hospital stay was 2.2 days. Renal cell carcinoma was confirmed in 34 patients (68%), and all patients had negative margins. There were few complications (12%) with 1 case of intraoperative hemorrhage, 1 case of delayed hemorrhage, and one urine leak.



**Figure 35.9** Laparoscopic partial nephrectomy. Intracorporeal laparoscopic suture repair of the violated urinary collecting system is completed using 4-0 polydioxanone suture.

Janetschek et al treated 98 patients with renal masses diagnosed by computed tomography (CT) scans that were T1 based on the 1997 TNM (tumor, node, metastasis) staging system.<sup>9</sup> The laparoscopic approach was used for all the patients with radical versus wedge resection determined by the tumor location, size, health, and age of patient and status of contralateral kidney. A wedge resection was performed in 25 patients with no conversions required. Both the transperitoneal (15) and retroperitoneal (10) approaches were used, depending on tumor location. No hilar control was obtained and hemostasis was achieved primarily with use of bipolar coagulation, argon beam, and fibrin glue as adjunctive measures. There were 3 complications, 2 of which involved a urine leak that required intervention. No tumors recurred over 22 months.

Harmon et al used laparoscopic coagulating shears for extended wedge resection in 15 patients.<sup>10</sup> Mean tumor size was 2.3 cm and both the transperitoneal (7) and

retroperitoneal (8) approaches were used. The renal vessels were dissected but not clamped. The argon beam coagulator (Birtcher Medical Systems, Ervin, California) was used to demarcate the renal capsule 1 cm beyond the tumor margin, and then the tumor was resected using the laparoscopic coagulating shears. The argon beam and oxidized cellulose gauze (Surgicel) were used for hemostasis. There were no complications associated with this procedure but blood loss was 500 ml or greater in 33% of the patients.

The clinical experiences and outcomes using coagulative techniques (RFA and microwave) are less mature. Gettman et al published a multicenter experience using RFA-assisted LPN. Ten patients underwent laparoscopically guided RFA with subsequent tumor excision.<sup>34</sup> The RITA or Radiotherapeutics device (RITA Medical Systems, Inc., Mountain View, CA) was employed (Figures 35.7 and 35.8). Mean tumor size was 2.1 cm. Median operative time was 193 min, and EBL was 198 ml (50–700). There were no perioperative complications, and negative margins were obtained in all cases.

Jacomides et al recently reported their experience with laparoscopic RFA followed by excision of tumor in 6 patients.<sup>28</sup> Mean tumor size was 1.8 cm. Mean operative time was 203 min and mean EBL was 80 ml. There were no perioperative complications and no urinary extravasation. A patient with the multiple treatments had a transient increase in creatinine from 1.3 to 1.8 mg/dl but this normalized within 2 weeks. Mean hospital stay was 2.5 days. Of the 6 patients, 1 patient had a focal positive margin that was felt to result from a technical error during excision. The patient had RFA 1 cm beyond the level of excision and was not re-explored. At 1-year follow-up, the patient remains recurrence free. Likewise, at a mean follow-up of 9.8 months there was no enhancement on CT scan in any of the patients.

**Table 35.2 LPN oncologic outcomes**

| Year | Author                        | Patients | Mean tumor size (cm) | Pathology   | Positive margin | Tumor recurrence | Mean follow-up (months) |
|------|-------------------------------|----------|----------------------|---|-----------------|------------------|-------------------------|
| 2002 | Gill et al <sup>8</sup>       | 50       | 3                    | RCC (68%), AML (16%), oncocytoma (10%), other (6%)            | 0               | 0                | 7.2                     |
| 2000 | Janetschek et al <sup>9</sup> | 25       | 1.9                  | RCC (76%), AML (4%), oncocytoma (4%), multilocular cyst (16%) | 0               | 0                | 22.2                    |
| 2001 | Stifelman et al <sup>11</sup> | 11       | 1.9                  | RCC (44%), AML (22%), benign cysts (33%)                      | 0               | 08               |                         |
| 2000 | Harmon et al <sup>10</sup>    | 15       | 2.3                  | RCC (80%), oncocytoma (20%)                                   | 0               | 08               |                         |
| 2001 | Gettman et al <sup>34</sup>   | 10       | 2.1                  | RCC (90%), AML (10%)  | 0               | NA               | NA                      |
| 2001 | Yoshimura et al <sup>14</sup> | 6        | 1.8                  | NA  | 1(17%)          | 0                | 3                       |

|                                      |    |     |                                   |    |   |    |
|--------------------------------------|----|-----|-----------------------------------|----|---|----|
| 2000 Rassweiler et al <sup>110</sup> | 53 | 2.4 | NA                                | NA | 0 | 36 |
| 1999 Hoznek et al <sup>7</sup>       | 7  | NA  | RCC (43%), AML (29%), other (29%) | 0  | 0 | 22 |
| 2000 Wolf et al <sup>6</sup>         | 10 | 2.4 | RCC (73%), benign (27%)           | 0  | 0 | NA |

AML=angiomyolipoma, RCC=renal cell carcinoma, NA=not available.

Yoshimura et al used the Microtaze OT-110M microwave generator in 6 patients.<sup>14</sup> The mean tumor size was 1.8 cm. Mean operative time was 186 min (range 131–239) and blood loss was minimal in all cases (less than 50 ml). There were no major complications. One patient had a positive margin on frozen sections that was subsequently treated with further laparoscopic resection. Limited follow-up of 3–4 months has detected no recurrences or metastatic disease. While hemostasis was effective, multiple needle placements may increase the error rates and lead to incomplete margin ablation.

### *New approaches*

Several new approaches have been presented recently that may simplify the performance of LPN.

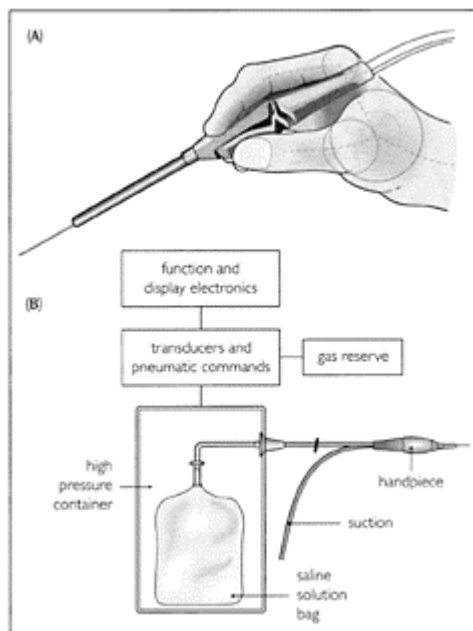
### **Water jet**

Basting et al recently reported their clinical experience and the histologic effects of a new water jet resection device on kidney tissue<sup>35,36</sup> (Figure 35.10A and 35.10B). A series of 24 patients underwent open surgery for renal cell carcinoma, nephrolithiasis, complicated cysts, or oncocytoma. The renal pedicle was exposed and controlled prior to resection. The renal capsule was incised and then the water jet was used to cut the parenchyma. A high-pressure pump is used to generate pressure between 16 and 22 bar that ‘jets’ water through a 0.12 mm pinhole. The high pressure allows the water jet to create a corridor in the desired dissection line without interfering with the intrarenal vessels and pelvicalyceal system. Resection took between 14 and 40 min with minimal intraoperative blood loss. The intrarenal vessels remained undamaged and could be ligated selectively. No significant postoperative complications occurred. Histologic evaluation demonstrated a sharp dissection line without thermal alterations or deep necrosis. Only a small disruption zone could be seen at the margins of the dissection.

### **Fibrin sealant powder**

Fibrin sealant powder (FSP) is a lyophilized human fibrinogen and thrombin preparation that can be applied as a dry spray through a gas-propelled device. Perahia et al randomized farm pigs to laparoscopic heminephrectomy using:

1. Conventional-bolstering sutures placed intracorporeally with vascular control using a pedicle clamp ( $n=13$ ); or
2. FSP application with regional ischemia using a laparoscopic kidney clamp ( $n=13$ )<sup>37</sup>.



**Figure 35.10** (A and B) Water Jet (Saphir Medical SA, Dardilly, France). The water jet resection device is a hand-held instrument used to cut through the renal parenchyma to resect renal lesions. A high-pressure pump generates high pressure that ‘jets’ through a 0.12 mm pinhole to slice through the renal parenchyma.

There were no differences in operating room (OR) time or blood loss between the groups. Urine extravasation was greater at 2 days in the FSP group but was nonexistent at 6 weeks. The authors found FSP application provides good hemostasis and eliminates the need for placing sutures. This application is awaiting clinical trials.

### Photopolymerized polyethylene glycol-lactide hydrogels

Photopolymerized polyethylene glycol (PEG)-lactide hydrogels have recently been evaluated for use as hemostatic barriers to limit parenchymal bleeding after LPN. Ramakumar and colleagues used a porcine model to perform wedge excision with vascular control and compare a ‘conventional’ strategy of ‘clamp and wait’ with application of hydrogels.<sup>38</sup> For the hydrogel group, primer and macromer were applied through laparoscopic ports. The hydrogel was polymerized on the cut surface of the

kidney using a green xenon light source, and the vascular pedicle clamp was released. The polymer gels remained adherent to the cut surface of the kidney with significantly less blood loss than the control group (2.5 ml vs 52.5 ml,  $p < 0.001$ ). No leakage or peeling of the hydrogel was observed at pressures up to 200 and 100 mmHg for ex-vivo vascular and retrograde ureteral perfusion, respectively. This application also awaits clinical trial.

### *Summary*

LPN is both safe and feasible for small renal tumors <4 cm. Exophytic tumors are ideal for resection using current technologies. While Gill et al have been successful in attaining vascular control and parenchymal suturing,<sup>8</sup> most other authors have attempted to simplify the operative technique by utilizing alternative means of hemostatic control. The use of the argon beam coagulator along with some form of gauze buttress to apply pressure is common and usually effective. Radiofrequency ablation followed by excision is a promising adjunct.

In general, tumor control has been good but awaits long-term follow-up to establish its equivalence with open techniques. However, morbidity is low overall, with short hospital stays for most series (see Tables 35.1 and 35.2).

## **Ablation**

In an attempt to decrease morbidity of surgical intervention for small renal tumors, tumor ablation has been evaluated for both laparoscopic and percutaneous approaches. For ablation to be effective, several factors must be addressed:

1. complete tumor destruction
2. safe, focused treatment
3. reproducible lesions
4. real-time monitoring of lesion formation
5. ability to determine treatment success.

While several energy modalities have been explored, cryotherapy and radiofrequency ablation have been the most extensively evaluated in both experimental and clinical settings. Other technologies such as high-intensity focused ultrasound, interstitial photon radiation energy, and ferromagnetic self-regulating reheatable thermal rod implants have also been evaluated.

## **Cryoablation**

Cryoablation is the most extensively utilized ablation technology. Multiple animal studies have evaluated the effects of cryoinjury on renal tissues<sup>39–50</sup> (Figure 35.11). The principle of cryoablation, as with any ablative technique, is precise localization of the renal tumor and complete destruction of the lesion without injury to adjacent structures.



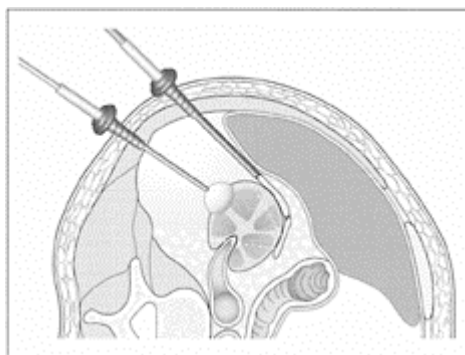
### *Technical aspects*

#### **Temperature**

Temperature plays a pivotal role in cell destruction during cryoablation. A temperature below  $-20^{\circ}\text{C}$  has been found to be important for cell death. Uchida et al evaluated renal cell lines by phase microscopy 24 hours after subjecting them to 60 min of temperatures of  $-5$ ,  $-10$ ,  $-20$  and  $-30^{\circ}\text{C}$ .<sup>51</sup> About 95% of renal cancer cells survived after cooling for 60 min at a temperature of about  $-10^{\circ}\text{C}$  but only 15% survived at a temperature of  $-20^{\circ}\text{C}$ . These findings were confirmed in a porcine model by Chosy et al, who demonstrated complete ablation of tumor at a temperature of  $-19.4^{\circ}\text{C}$ ,<sup>48</sup> and by Schmidlin and colleagues, who found the threshold temperature for complete tissue ablation to be  $-16.1^{\circ}\text{C}$ .<sup>45</sup>

#### **Ice ball size**

In order to guarantee complete ablation, it is important to extend the ice ball a sufficient distance beyond the tumor borders. The margin of cell death beyond the probe is an important consideration in deciding the depth of probe deployment. Campbell and coauthors demonstrated that a temperature less than  $-20^{\circ}\text{C}$  was achieved 3.1 mm behind



**Figure 35.11** Laparoscopic renal cryosurgery. Laparoscopic renal cryosurgery is performed with a retroperitoneal access and laparoscopic intraoperative ultrasonic guidance.

the leading edge of the ice ball.<sup>39</sup> The fact that temperatures sufficient for cell death were found in close proximity to the probe suggests that the cryoprobe does not need to be inserted far beyond the tumor edge to obtain a negative margin.

### Freeze-thaw cycle

Initial researchers used a single freeze-thaw cycle<sup>48</sup> to destroy tumor cells. However,<sup>45,51,52</sup> most current clinical series have utilized double freeze-thaw cycles<sup>53</sup> to ensure greater tumor destruction.<sup>54–56</sup>

While there is concern that vascular flow to the kidney may affect the freezing of tissue, renal artery occlusion does not significantly alter the freezing process and provided no practical advantage in an animal model.<sup>39</sup>

### Monitoring

### Imaging

Due to the destructive nature of the ice ball, it is important to monitor the extent of the lesion as it develops. Direct vision is not a sufficient predictor of tissue destruction, with incomplete ablation noted in 11% of samples taken within the visible margins of the iceball.<sup>48</sup> Real-time ultrasound, including intraoperative laparoscopic ultrasound, has been utilized to monitor the ice ball<sup>46,53–57</sup> (Figures 35.12 and 35.13). The evolving renal ice ball is visualized as a hyperechoic, crescentic advancing edge with posterior acoustic shadowing.<sup>47</sup> On the other hand, renal tumors are mildly hyperechoic or of mixed echogenicity and the renal sinus fat is hyperechoic. The ultrasound probe is placed



**Figure 35.12** Laparoscopic renal cryosurgery. An ultrasound image of a cryoablation probe being placed into a renal lesion. (Courtesy of Tung Shu.)

opposite the tumor, allowing precise placement of the cryoprobe up to the deep margin of the tumor. Zegel et al found that intraoperative ultrasonography accurately delineated tumor size, cryoprobe placement, and depth of freezing.<sup>58</sup> An echogenic interface was generated by the marked differences at the junction of the normal renal parenchyma and frozen tissue.

Open magnetic resonance imaging (MRI) has also been used to monitor iceball formation during percutaneous cryoablation.<sup>44,59,60</sup> The advantages of MRI include a three dimensional view with good soft tissue imaging. The iceball is seen as a signal void on T1-weighted images. MRI has the advantage of allowing imaging distal to the iceball, achieved secondary to the iceball acoustic shadowing effect.<sup>46,56,57</sup>

### *Outcome*

### **Histology**

Multiple animal studies have evaluated histologic changes as a result of cryoinjury. Acutely, cryoinjury results in sharply demarcated lesions with minimal inflammation<sup>41</sup> (Figure 35.14). At 1 week, four distinct zones are seen: central necrosis, inflammatory infiltrate, hemorrhage, and fibrosis with regeneration. At 13 weeks, the necrotic tissue is replaced with a circumscribed area of fibrosis.<sup>46,49</sup> These findings have been confirmed in human renal tumors.<sup>52</sup>

### **Radiology**

Both CT and MRI have been used to follow-up patients after cryoablation. Gill and Novick use MRI for follow-up



**Figure 35.13** Laparoscopic renal cryosurgery. An ultrasound image of an 'ice ball'; a hypoechoic lesion created by cryosurgical ablation of a renal lesion. (Courtesy of Tung Shu.)



**Figure 35.14** Laparoscopic renal cryosurgery. Gross pathologic renal specimen demonstrates acute post-surgical changes of a renal lesion and surrounding parenchyma. (Courtesy of Tung Shu.)

and noted that the primary criterion for successful cryoablation is nonenhancement of lesions after gadolinium administration.<sup>61</sup> All cryolesions are isointense to the adjacent normal parenchyma on T1-weighted images and hypointense on T2-weighted images. On day 1, half the cases may have a hyperintense peripheral rim at the border of the cryolesion and normal kidney. On day 30, the cryolesions demonstrate an increase in signal intensity on both T1- and T2-weighted images but no enhancement.<sup>56</sup> MRI also demonstrates sequential contraction of the cryolesion.<sup>55</sup> The disadvantage of radiologic follow-up, however, is that most cryolesions do not resolve completely.<sup>57,62</sup>

### Clinical series

There have been multiple clinical series evaluating cryotherapy. These series, however, have been limited by relatively short follow-up (<3 years) and small numbers of patients. The patients have for the most part been selected carefully to include small (<4 cm), peripheral lesions. Most have been approached laparoscopically but the percutaneous<sup>51</sup> and open approaches have also been utilized. Table 35.3 summarizes the results of these trials.

Rukstalis performed open renal cryoablation on 29 patients with a median preoperative lesion size of 2.2 cm.<sup>63</sup> Five serious adverse events occurred in 5 patients, with only 1 event directly related to the procedure. One patient experienced a biopsy-proven local recurrence, and 91.3% of patients (median follow-up 16 months) demonstrated a complete radiographic response with only a residual scar or small, nonenhancing cyst.

Bishoff et al treated 8 patients with small (average 2 cm) exophytic renal masses.<sup>46</sup> They underwent laparoscopic biopsy and cryosurgical ablation using a 3 or 4.8 mm probe (Cryomedical Sciences Inc., Rockville, Maryland) for one 15 min or two 5 min freeze cycles to a temperature of  $-180^{\circ}\text{C}$ ; the ice ball was extended at least 7 mm beyond the

tumor margin.<sup>46</sup> There were no intraoperative or postoperative complications in the 8 patients. The estimated blood loss was 140 ml, and the mean hospital stay was 3.5 days. At a mean clinical follow-up of 7.7 (range 1–18) months and radiographic follow-up of 5 months, there have been no tumor recurrences or significant changes in the serum creatinine concentration.

The Cleveland Clinic group have one of the larger experiences with cryoablation and have published their series with initial and intermediate results.<sup>55,56,64</sup> Sung et al reported the intermediate follow-up results of laparoscopic renal cryoablation in 50 patients (34 tumors) with a mean tumor size of 2.1 cm.<sup>64</sup> As dictated by the tumor location, cryoablation was performed by either the retroperitoneal ( $n=38$ ) or the transperitoneal ( $n=12$ ) laparoscopic approach using real-time ultrasound monitoring. A double freeze-thaw cycle was routinely performed. The mean surgical time was 2.6 hours, cryoablation time 20.5 min, and blood loss 50.6 ml. For a mean intraoperative ultrasonographic tumor size of 2.1 cm, the mean cryolesion size was 3.5 cm. Sequential MRI demonstrated a gradual contraction in the mean diameter of the cryolesions with complete resolution in 9 patients with 2-year follow-up. Of 31 patients who underwent CT-guided biopsy at 3–6 months, 30 had negative biopsies. One patient had a 1.3 cm heterogeneous enhancing nodule on 18-month MRI and underwent a nephrectomy based on a positive needle biopsy.

Shingleton and Sewell have reported in several studies on the feasibility and safety of performing percutaneous cryoablation of renal tumors using open MRI.<sup>49,59,60</sup> They recently reported their 1-year follow-up with a total of 35 patients with mean tumor size of 3.7 cm. Patients were hospitalized overnight for observation. Follow-up imaging with MRI or CT and physical examinations were done at 1 week, and at 1, 3, 6, and 12 months. Complications occurred in 5 patients: a superficial wound abscess in 1, self-limiting gross hematuria in 4. At mean follow-up of 12 months, all patients were alive with no evidence of residual or new tumors. Five patients underwent retreatment for residual enhancing mass.

Harada et al also evaluated the feasibility of performing percutaneous cryosurgery, treating 4 patients with renal tumors with local anesthesia using a horizontal open MRI system (AIRIS II, Hitachi Medical Corp., Tokyo, Japan).<sup>65</sup> Mass size was radiographically documented as 4 cm or less in diameter. A 2 or 3 mm cryoprobe was advanced into the renal mass under real-time MR monitoring. Follow-up dynamic CT and physical examination were done after 2 weeks and 6 weeks. Cryoablated tumors resolved, and there were no serious complications and no clinically significant changes during the procedures and follow-up study.

**Table 35.3 Ablation series**

| Tech<br>nique                    | Year Aut<br>hor                     | Pat<br>ients<br>(tum<br>ors) | Mean tumor<br>size<br>(cm) | Succ<br>essful<br>ablation <sup>a</sup> | Mean<br>foll<br>owup<br>(months) | Major<br>comp<br>lication | Minor<br>comp<br>lication | LOS<br>(days) | Hist<br>ology |
|----------------------------------|-------------------------------------|------------------------------|----------------------------|---|----------------------------------|---------------------------|---------------------------|---------------|---------------|
| Laparo<br>scopic<br>cryoablation | 2001 Sung et al <sup>64</sup>       | 50                           | 2.1                        | 30/31<br>(97%) <sup>c</sup>             | 18.8                             | NA                        | NA                        | NA            | NA            |
| Laparo<br>scopic<br>cryoablation | 1999 Bishoff et<br>al <sup>46</sup> | 8                            | 2                          | 8/8<br>(100%)                           | 7.7                              | 0                         | 0                         | 3.5           | NA            |

|   |  |         |       |   |                |                                       |  |                                |   |
|---|--|---------|-------|---|----------------|---------------------------------------|--|--------------------------------|---|
| Laparoscopic cryoablation                   | 2002 Kmi et al <sup>111</sup>            | 12      | 2.2   | 10/12 (83%)                                     | 10             | NA                                    | NA   | 3.25                           | 8/12 RCC  |
| Laparoscopic (n=3)/ Open (n=4) cryoablation | 2000 Rodriguez et al <sup>57</sup>       | 7       | 2.2   | 6/7 studied with partial resolution (no growth) | 14             | 0                                     | Pelvic vein thrombosis, worsening of CVA symptoms (resolved)                                 | 4.4                            | 5/7 RCC, 2/7 indeterminate                                  |
| Percutaneous cryoablation                   | 2001 Shingleton and Sewell <sup>49</sup> | 35      | 3.7   | 30/35 (86%)                                     | 12             | 0                                     | Gross hematuria (n=4), wound infection (n=1)   | NA                             | NA  |
| Percutaneous cryoablation                   | 2001 Harada et al <sup>65</sup>          | 4       | <4    | 4/4 (100%)                                      | 1.5            | 0                                     | NA   | NA                             | NA  |
| Percutaneous RF ablation                    | 2001 McGovern et al <sup>91</sup>        | 17 (19) | 1–5.5 | 15/18 (84%)                                     | 6–36           | No                                    | Ureteral obstruction requiring 3 stent (n=2) and gross hematuria /perinephric bleeding (n=1) | 15/18 outpatient, 3 admissions | RCC   |
| Percutaneous RF ablation                    | 2000 Gervais et al <sup>90</sup>         | 8(9)    | 3.3   | 7/9 (78%)                                       | 10.3           | Large perinephric hematoma and anuria | Reaction to fentanyl   | 12/14 outpatient, 2 admissions | RCC (n=7)   |
| Percutaneous RF ablation                    | 2002 Pavlovich et al <sup>89</sup>       | 21(24)  | 2.4   | 19/24 (79%)                                     | 2              | No                                    | Pain on hip flexion (n=2), flank numbness (n=2)  | 1                              | Known VHL (n=19) or hereditary papillary renal cancer (n=2) |
| Percutaneous RF ablation                    | 2002 Ogan et al <sup>81</sup>            | 13      | 2.4   | 12/13 (93%)                                     | 2.9            | No                                    | Perinephric hematoma (n=1)   | 0.9                            | Biopsy in 5 patients: RCC (40%) onco cytoma (40%) AML (20%) |
| Percutaneous RF ablation                    | 2002 de Baere et al <sup>112</sup>       | 5       | 3.3   | 5/5 (100%)                                      | 9 <sup>b</sup> | NA                                    | Hematuria (n=2), subcapsular hematoma (n=1)  | 1.8                            | RCC (biopsy proven prior to treatment)                      |
| Laparoscopic RF ablation                    | 2002 Jacomides et al <sup>28</sup>       | 8(11)   | 2.1   | 8/8 (100%)                                      | 9.8            | No                                    | No   | 1.5                            | RCC (75%), AML (12.5%), oncocytoma (12.5%)                  |

<sup>a</sup> Successful ablation defined as no contrast enhancement on follow-up CT imaging.

<sup>b</sup> Median.

<sup>c</sup> Negative CT-directed biopsy at 3–6 months. AML=angiomyolipoma, RCC=renal cell carcinoma, NA=not available, LOS=length of stay, RF=radiofrequency, CT=computed tomography, CVA=cerebrovascular accident, VHL= Von Hippel-Lindau disease.

## Complications

**Bleeding.** A concern with cryoablation is bleeding at the probe site and from cracks in the parenchyma during thawing. In an animal study, Nakada et al noted a crack in the renal parenchyma of one kidney during the thaw phase; at harvest that animal was found to have an intraperitoneal hemorrhage.<sup>43</sup> Rodriguez and coauthors routinely packed the probe site with microfibrillar collagen hemostat and applied pressure for 2–3 min in addition to using the argon beam coagulation as necessary to control bleeding.<sup>57</sup>

**Injury to collecting system.** Campbell et al. observed an obstructive stricture of the ureteropelvic junction in 1 animal after cryotherapy.<sup>39</sup> Barone and Rodgers performed cryoinjury on white rabbits with solitary kidneys using a liquid nitrogen probe.<sup>40</sup> Transient gross hematuria was noted in 25% of the animals and microscopic hematuria in 50%. In an interesting study presented by Sung, cryolesions were intentionally extended to the collecting system and unless the cryoprobe physically penetrated the calyces, the collecting system healed in a water tight fashion.<sup>66</sup>

**Effect on renal function.** Barone and Rodgers performed cryoinjury on white rabbits with solitary kidneys.<sup>40</sup> Serum blood urea nitrogen and creatinine levels reached maximum levels at 72 hours and gradually returned toward normal thereafter. Carvalhal et al. followed 22 patients after laparoscopic renal cryoablation for a minimum of 6 months.<sup>67</sup> No significant differences were found between the preoperative and latest postoperative serum creatinine (sCr) levels (1.13 and 0.91 mg/dl, respectively), systolic and diastolic blood pressure values (135.6 vs 131.2 mmHg and 78 vs 72.7 mmHg, respectively), or in the estimated creatinine clearance. The number or dose of antihypertensive medications did not change during the follow-up period for any patient. In 3 patients with a solitary kidney, the blood pressure and sCr values remained unchanged (mean preoperative sCr 1.43 mg/dl, and mean postoperative sCr after a minimum of 6 months 1.33 mg/dl). Laparoscopic renal cryoablation did not have a deleterious impact on renal function or blood pressure during a mean follow-up of 20.6 months.

## Summary

Cryoablation has shown good results, with relatively few complications and low morbidity. Long-term follow-up is necessary to demonstrate oncologic control. At this time, percutaneous cryoablation is limited by the availability of open MRI.

## Radiofrequency ablation

RFA has been shown to be an effective and safe method for destroying living tissues (see Figures 35.7 and 35.8). Energy generated by the RF probes creates temperature to >

100°C and induces coagulative necrosis in tissues. This technology has been used in multiple organs, including liver,<sup>68</sup> nerves,<sup>69,70</sup> bone,<sup>71</sup> prostate,<sup>72–75</sup> and heart.<sup>76–79</sup>

Zlotta and colleagues were the first to evaluate this technology for renal tumors.<sup>80</sup> They used a RITA generator and measured power delivery, impedance, and total energy delivered. Initially, 4 ex-vivo kidneys were treated. Then, 2 patients with localized renal cancer were treated immediately prior to nephrectomy and 1 patient received percutaneous treatment 1 week prior to nephrectomy. In the patient with the RITA treatment 1 week prior to nephrectomy, the kidney demonstrated extensive coagulative necrosis with no residual tumor cells. No damage was seen beyond the target lesion. The CT scan after 1 week of treatment demonstrated absence of contrast in the targeted lesion. Importantly, several parameters concerning RF were established:

1. the lesions observed were similar to lesions that were forecast
2. the dimensions of thermal lesions created by RF could be monitored by tissue impedance, power delivery, time of application, and total energy delivered to the tissues
3. the treatment is safe and reproducibly destroyed renal tissue
4. the CT scan is an effective modality for following lesions after treatment
5. ultrasound is not effective in assessing lesions during ablation.

### *Indications*

As with most nephron-sparing procedures, RFA is limited to small lesions and is best for exophytic lesions. Endophytic lesions raise concerns about injury to the collecting system and hilar structures, whereas large lesions (>4 cm) are difficult to ablate completely with the current technology.

### *Techniques*

#### **Approach**

The surgeon's preference should always be the primary decision-making tool in determining the approach for RFA. Anterior lesions are easier to approach transperitoneally, but posterior and lateral lesions can be treated from either a retroperitoneal or transperitoneal approach. For percutaneous ablation, it is important to determine if the bowel or lung will limit percutaneous access. Whereas the morbidity of percutaneous approaches is less than for the laparoscopic approach, tumor position in relation to adjacent organs is critical in determining the safety of percutaneous RFA. Ogan et al had to change the management of 3 patients initially scheduled for percutaneous RFA to a laparoscopic approach due to inability to safely guide the needle using a CT scanner.<sup>81</sup>

#### **Radiofrequency generators**

There are temperature- and impedance-based RF generators. The RITA system is a temperature-based system and delivers energy at 150 W until the average temperature at



the various prongs averages at over 100°C. The Radiotherapeutics device delivers energy up to 200 W. Typically, an ablation cycle starts at 50 W, with an increase of 10 W each minute to a maximum of 90 W. This setting is maintained until impedance has reached 200 ohms, at which time power passively decreases to less than 10 W. Both manufacturers recommend repeating the treatment cycle. Conceptually, temperature-based probes generate a temperature above that necessary to destroy the tumor cells and monitor this temperature level. Impedancebased probes generate energy that enters the tissues and the impedance rises when the tissue is charred and no more energy can be transferred, which signals successful treatment.

In a porcine model, when the 2 probes were compared using manufacturer recommendations, they generated similar-sized lesions with no viable cells.<sup>82</sup>

### **‘Wet’ radiofrequency ablation**

During RFA, desiccation of tissue causes a rise in impedance, which limits the amount of energy that is delivered to tissues. Infusion of saline into the treatment area can limit early desiccation of tissue around the needle tip and allow greater delivery of energy.

Polascik and colleagues studied the use of an RF electrode (RFT system; United States Surgical Corp., Norwalk, Connecticut) with a continuous 14.6% saline infusion (2 ml/min).<sup>83</sup> A VX-2 tumor was implanted in 14 rabbit kidneys and treatments of 30 or 45 s were applied prior to sacrifice. Mean lesion sizes increased from 1.4 cm×1.0 cm to 1.8 cm×1.5 for the 30 s and 45 s treatment groups. No acute complications were noted.

In another study of ‘wet’ RFA, Patel and colleagues infused 14.6% saline at 10 ml/min for 15 s into normal renal parenchyma of New Zealand white rabbits prior to ablation.<sup>84</sup> Fifty watts of energy were delivered at 475 kHz for 1 or 2 min. There were no complications in 48 treated animals with no fistula/urinoma and no perinephric hematomas. Treatments for 1 min and 2 min created average lesions of 7 cm<sup>3</sup> and 10 cm<sup>3</sup>, respectively. Impedance did not limit the delivery of energy during the treatments.

Although ‘wet’ RFA may allow larger lesion formation, most current studies have used ‘dry’ RFA.

### *Histology*

Zlotta et al evaluated acute and 1-week histologic changes after RFA.<sup>80</sup> Macroscopic discoloration was noted in all specimens treated. Microscopic lesions were consistent with intense stromal and epithelial edema as well as hypereosinophilia and pyknosis. In a patient with the RITA treatment 1 week prior to nephrectomy, the kidney demonstrated extensive coagulative necrosis with no residual tumor cells.

Rendon et al also noted significant acute cellular effects, including cytoplasmic vacuolization, chromatic condensation, and cellular shape changes after RFA.<sup>85</sup>

Corwin et al performed laparoscopic RFA in 11 farm pigs,<sup>86</sup> and acute hematoxylin and eosin (H&E) staining revealed preserved renal parenchymal architecture with only minimal cellular changes. However, nicotinamide adenine dinucleotide staining (NADH) for metabolic activity demonstrated complete cell death.

To assess the chronic histologic changes of RFA, Hsu et al performed RFA on 11 pigs, with 5 survival animals.<sup>87</sup> Initially, lesions show intense inflammation and

coagulative necrosis. Subsequently, there was near total resorption of the necrotic foci by day 90.

### *Radiologic monitoring*

Unlike cryoablation, real-time monitoring of RFA is not possible. Several investigators have noted that ultrasound was useful for needle placement but could not accurately demonstrate the region of treatment.<sup>80,86,88</sup> For percutaneous RFA, ultrasound and CT scan can be used for localization. Ogan et al have noted the importance of deploying the probe approximately 0.5–1.0 cm beyond the CT-measured tumor diameter for effective cancer control.<sup>81</sup>

Post-procedure, CT scan and MRI are effective in evaluating lesions for follow-up. Loss of lesion enhancement is the key to evaluating for successful treatment.<sup>80,81,88</sup> CT scanning often reveals either spherical lesions or wedged shaped regions, suggesting intrarenal vascular injury leading to segmental infarction.<sup>88,89</sup>

### *Hilar occlusion*

With the goal of evaluating the effects of hilar occlusion on the extent of RFA, Corwin et al performed laparoscopic RFA in 11 farm pigs.<sup>86</sup> They used the RITA probe and delivered 50 W with average temperature of 100°C for 8 min. There were no perioperative complications or urinoma formations. Lesions formed were symmetrical with a rounded, spherical contour. The lesion dimensions were larger in the hilar occlusion group, but this was not statistically significant.

### *Outcomes*

#### **Clinical series**

Table 35.3 summarizes the outcome of treatment with RFA. Tumor sizes mostly range from 2–3 cm and follow-up was less than 2 years for most series. Success was primarily defined as no enhancement on surveillance imaging and ranged from 78 to 100%.

Gervais and colleagues performed percutaneous RFA in 8 patients.<sup>90</sup> This preliminary experience was limited to patients with life expectancy shorter than 10 years, significant comorbidities, and/or a solitary kidney. A total of 9 tumors were treated in these 8 patients, with diagnosis based on needle biopsy ( $n=7$ ), enlarged enhancing renal mass with 2 nondiagnostic biopsies ( $n=1$ ), and enlarged enhancing mass on MRI ( $n=1$ ). All procedures were performed with intravenous (IV) sedation (RF generator: Cosman Coagulator CC-1; Radionics, Burlington, Massachusetts). Follow-up was performed using CT and MRI at 1, 3, and 6 months. Four patients were treated in one ablation session and 4 required more than one session because of imaging evidence of a residual tumor. All 5 exophytic and all 3 small tumors (<3 cm) were free of enhancement at 6 months. Only 1 of the 3 central tumors was free of enhancement. No patients developed metastases or renal insufficiency. The authors found that centrally located and larger tumors were more difficult to treat and, in fact, the 2 failures occurred in tumors the size of 4.4 and 5 cm despite several repeat treatments.

Pavlovich et al recently published their initial experience with RFA in 21 patients with known VHL (Von Hippel-Lindau disease) or hereditary papillary renal cancer and <3 cm solid renal masses.<sup>89</sup> Twenty-four tumors were treated percutaneously using conscious sedation. The RITA Starburst XL probe was used to deliver 50 W with temperature set to 100°C for a minimum of two 10–12 min cycles. A third cycle was applied for deep medullary tumors and those close to 3 cm. Of the 24 treatments, 19 were considered satisfactory, based on accurate targeting and maintenance of >70°C temperature at all probe electrodes during therapy. Results were based on a follow-up CT scan at 2 months. Of the 24 lesions, 5 had focal areas of persistent growth enhancement. While 4 of the 5 were believed to have been insufficiently treated, 1 lesion fulfilled the criteria for a satisfactory treatment.

McGovern et al also performed percutaneous RITA for 19 RCC in a total of 17 patients.<sup>91</sup> These were done in an outpatient setting using IV sedation with an internally cooled RF electrode. Tumor sizes ranged from 1 to 5.5 cm, with follow-up ranging from 6 months to 3 years. There was complete response in 15 of 18 patients and partial response in 3 patients.

Ogan et al recently reported on 12 patients with 13 tumors who underwent percutaneous RFA.<sup>81</sup> To qualify for treatment, lesions were <4 cm, posterior or lateral in location, and enhancing on imaging studies. Mean tumor size was 2.4 cm. A RITA Starburst XL probe was deployed approximately 0.5–1.0 cm beyond the CT-measured tumor diameter. Target temperature was 105°C and tumors were treated for one or two 5–8 min cycles based on surgeon preference. There were no major complications and 1 patient developed a small perinephric hematoma. Mean length of stay was 0.9 days. Twelve of the 13 patients demonstrated complete ablation on the most recent CT scan, with mean follow-up of 4.9 months.

Despite 2 case reports of laparoscopic RFA, experience lags behind that with percutaneous treatment. Jacomides et al recently reported the only series of laparoscopic RFA on 8 patients.<sup>28</sup> A RITA Starburst XL probe was deployed to ablate a volume approximately 0.5–1.0 cm beyond the CT-measured tumor diameter. Eleven tumors were treated with mean size of 2.1 cm. Mean operative time was 140 min. There were no perioperative complications and no urinary extravasation. Mean hospital stay was 1.5 days. With a mean follow-up of 9.8 months there was no enhancement on CT scan in any of the patients.

### **Effect on renal function**

Gill and colleagues used a porcine model to evaluate acute and chronic changes that resulted from performing bilateral RFA of kidneys.<sup>92</sup> Serum creatinine remained stable at 90 days despite bilateral RFA.

No series published at this time has found significant changes in serum creatinine.<sup>81,89,90</sup>

### **Injury to adjacent structures**

RFA can cause thermal injury to adjacent structures, such as the psoas muscle<sup>88,93</sup> and bowel.<sup>93</sup> In an effort to evaluate ways to protect surrounding structures from thermal

injury during RFA, Rendon et al studied the use of hydroand gas-dissection in the perirenal space.<sup>93</sup> In 3 pigs, a 13-gauge cannula was inserted percutaneously under ultrasound guidance and positioned under Gerota's fascia with a total of 30–60 ml of sterile saline injected to create a fluid space. In 2 pigs, a 22-gauge venous access catheter was used to infuse 500 ml of CO<sub>2</sub> under Gerota's fascia. These techniques prevented injury to adjacent structures. A disadvantage of the CO<sub>2</sub>, however, was interference with ultrasound. These techniques have important clinical implications since the threat of injuring anterior structures such as bowel is an important consideration in planning appropriate treatment of renal lesions.

Pavlovich et al noted pain on hip flexion ( $n=2$ ) and cutaneous flank numbness ( $n=2$ ) after percutaneous RFA. The pain on flexion resolved within 2 weeks but the numbness persisted at 2 months.<sup>89</sup>

Injury to the collecting system can result in hematuria.<sup>89,91</sup> Fortunately, this can usually be managed conservatively. Perinephric bleeding is not uncommon and has been noted in several series.<sup>81,90,91</sup> Rarely, patients may need a blood transfusion.<sup>90</sup>

### **Incomplete treatment**

Despite the promising results, one of the criticisms of ablation technology is the uncertainty of complete tumor destruction. In a related study, Rendon and coauthors evaluated nephrectomy specimens after RFA.<sup>85</sup> Ten patients with <3.5 cm renal masses underwent RFA using a LeVeen electrode (Radiotherapeutics Corp., Sunnyvale, California) prior to a partial nephrectomy or with ultrasound/CT guidance in a group treated 7 days prior to open surgery. In several cases it was concluded that viable tumor persisted in 5–10% of the volume. In 2 of these patients, a CT scan did not demonstrate enhancement at 7 days post-treatment. All the areas of tumor positivity occurred at the margins of the lesions and not the center. Several important points are noted from this study. First, RFA depends on appropriate probe placement and ablation of a margin of normal renal parenchyma around the tumor. It is possible that variability in blood flow may allow tissue at the margins to remain viable so the RF probe needs to be deployed >0.5 cm beyond the tumor margin. Secondly, the CT scan may not be accurate at 1 week post-treatment and may take longer to demonstrate enhancement with residual tumor. Finally, H&E staining is not sufficient to assess viability, whereas NADH staining has been shown to more accurately establish metabolic activity in tissues.

Large tumors and centrally located tumors increase the risk of inadequate treatment with RFA because of technical problems with appropriate positioning of the probes to provide adequate treatment to the periphery of the tumors. McGovern et al had an incomplete response in 3 patients with tumors greater than 3.5 cm.<sup>91</sup> Gervais et al found that only 1 of the 3 patients with central tumors was free of enhancement. These tumors were 4.4 and 5 cm in size and were unresponsive despite several repeat treatments.<sup>90</sup>

### *Conclusion*

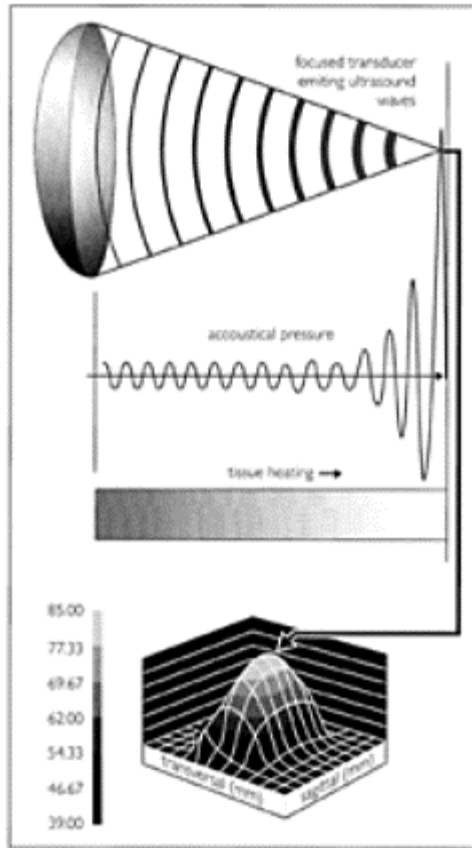
RFA offers a promising modality for managing small renal tumors laparoscopically or percutaneously. Initial results are favorable but long-term results are necessary to evaluate oncologic control.

### High-intensity focused ultrasound

High-intensity focused ultrasound (HIFU) uses focused ultrasound waves that are generated by a cylindrical piezoelectric element to create heat in tissues (Figure 35.15). A parabolic reflector focuses the ultrasound waves, and the ultrasound is coupled by degassed water between the source and the patient's skin. In a manner similar to extracorporeal shock wave lithotripsy, the sound waves penetrate the skin, with only slight absorption, prior to converging on the focus point. A high power density, exceeding  $100 \text{ W/cm}^2$ , can achieve temperatures above  $65^\circ\text{C}$  within a pulse duration of less than 5 s.<sup>94</sup> The size of the ablated tissue is similar to the focal zone but can be controlled by the power and duration of ultrasound pulses.<sup>94</sup> Tissue destruction occurs as a result of both thermal and mechanical (cavitation) effects.

HIFU has been utilized for various clinical applications, from treatment of glaucoma<sup>95</sup> to liver<sup>96</sup> and prostate tissue ablation.<sup>97</sup> Experimental applications in animals have been performed to evaluate HIFU effects on renal tissues.<sup>28,98–102</sup> Chapelon and colleagues used a 1 and 2.25 MHz transducer to perform in-vivo tissue destruction on 124 rat and 16 canine kidneys.<sup>98</sup> The rat experiments were used to define the constants necessary to produce a localized tissue lesion at the focus of the transducer. Subsequently, in the canine experiments, extracorporeal HIFU was performed and kidney lesions were achieved in 10 animals (63%). These lesions were histologically determined to be coagulation necrosis.

Watkin et al performed HIFU in 18 porcine kidneys.<sup>103</sup> No macroscopic lesions were detected in 5 kidneys. In 13 kidneys, 67% of total shots fired were detected within the target area. Lesion sizes ranged from 4 to 17 mm in length and 0.5 to 2.5 mm in width. Individual lesions were well circumscribed with a pale central area surrounded by a hemorrhagic rim. Histologically, in the central zone, tubules were obliterated and nuclei were pyknotic and hyperchromatic. In the periphery, the tubules were



**Figure 35.15** High-intensity focused ultrasound (HIFU). Focused ultrasound waves generated by a piezoelectric element create heat in tissues. A parabolic reflector focuses the ultrasound waves, and the ultrasound is coupled by degassed water between the source and the patient's skin. The sound waves penetrate the skin with only slight absorption, prior to converging on the focus point tumor. Tissue destruction occurs as a result of both thermal and mechanical effects.

distended and filled with amorphous material, and the nuclei were hyperchromatic but not significantly pyknotic. Due to anatomic constraints such as rib interference, only the lower pole could be treated. There was an acute skin burn in 1 animal and skin changes with red discoloration in 9 other treatments.

Paterson and colleagues developed a probe that allows for HIFU application laparoscopically.<sup>104</sup> They directly applied HIFU to renal tissue in a porcine model ( $n=13$ ) and created lesions in 12 of 13 kidneys. There were no significant complications, and they achieved homogenous lesions with complete tissue necrosis throughout the entire volume.

There have been few human applications of HIFU for renal tissue. Susani et al performed HIFU in 2 patients prior to radical nephrectomy.<sup>105</sup> Hemorrhagic necrosis was found in the specimens but the amount of tumor necrosis did not allow recognition of the treatment zone.<sup>105</sup> Vallancien et al. performed phase I and II studies in patients with renal tumors.<sup>28,101,102</sup> Four patients with T2 and T3 kidney tumors were treated 2, 6, 8, and 15 days prior to nephrectomy. The final pathology revealed coagulative necrosis in the targeted areas. There was a second-degree skin burn in 1 patient due to an error in dosimetry. Kohrmann et al presented the first report on a patient with renal cell carcinoma who underwent HIFU with curative intent.<sup>94</sup> HIFU was applied to 3 tumors in 3 sessions with the patient under general anesthesia or sedation analgesia, followed by MRI for 6 months. General anesthesia was required to apply high-energy levels of focused ultrasound. After treatment, MRI showed necrosis in the 2 tumors in the lower kidney pole within 17 and 48 days, respectively. The necrotic tumor area shrank thereafter but at 6 months did not completely disappear. The tumor in the upper pole was not affected by treatment because the ultrasound energy was absorbed by the interposed ribs. Successful HIFU application depended on optimum energy coupling, a sufficiently high ultrasound energy level, and general anesthesia.

HIFU is still an experimental modality with little clinical history. A better method for focusing energy is needed to avoid skin burns and other complications. Furthermore, studies need to prove that HIFU provides complete tissue destruction before it is used for cancer control.

### **Interstitial photon radiation energy**

Interstitial photon radiation energy uses a probe to deliver controllable local radiation therapy without exposing intervening layers of tissue. A miniature X-ray generator device produces low-energy X-ray photons, which attenuate rapidly in tissues, resulting in sharply defined boundaries. This technology was evaluated in 12 dogs and 11 renal lesions were generated.<sup>106</sup> The lesions were well demarcated and demonstrated coagulative necrosis that organized into fibrosis over time. There were no hematomas or urinomas. A single 10 min treatment (15 Gy at a radius of 1.3 cm) resulted in a 2.5 cm lesion. Further studies are necessary to evaluate this technology's potential.

### **Interstitial laser thermoablation**

Laser ablation of target tissue using one or several laser fibers has been described in the treatment of head and neck, liver, brain, and kidney tumors as well as the treatment of benign prostate hyperplasia and uterine fibroids.

Using MR-guided interstitial laser thermoablation (ILT), de Jode et al treated kidney tumors in 3 patients. Laser energy from a neodymium:YAG source was percutaneously delivered to the tumors under real-time MR guidance in an open access scanner. Follow-up gadolinium-enhanced MRI confirmed necrosis in the target tissue. One patient showed areas of enhancement consistent with viable tumor and underwent an additional ablation of the enhancing areas.<sup>107</sup>

In a porcine model, Gettman et al studied the size and histology of lesions created with interstitial laser coagulation (ILC) via a laparoscopic approach with and without hilar occlusion in the porcine model.<sup>108</sup> For each kidney, a 600  $\mu\text{m}$  bare-tip silicon laser fiber was attached to a diode laser (wavelength=805 nm) and inserted 0.5 cm into the lower pole for 15 min at 6 W. Histology revealed cellular inflammation in acute lesions; chronic lesions demonstrated coagulative necrosis with progressive fibrosis. NADH staining showed viable cells within the treatment zone of surviving animals.

The histologic evidence of viable cells within the treatment zone suggests that additional refinement of the ILC technique in the animal model is warranted before further application in humans.

### **Ferromagnetic thermal rod implants**

Rehman and colleagues evaluated the use of ferromagnetic self-regulating reheatable thermal rod implants for in-situ tissue ablation.<sup>109</sup> Ferromagnetic compounds, when placed in a magnetic field, develop an electric current. In tissue, the ferromagnetic compounds meet resistance to transmission of the current, leading to heat generation. The goal of the study was to evaluate the effect of permanently implanting palladium and cobalt rods that self-regulate to 70°C in solid abdominal organs. In 16 pigs, renal, hepatic, uterine, and pancreatic rods were placed in 1 cm parallel rows to ablate 7 g of tissue. The animals were treated in an extracorporeal magnetic field of 50 gauss rms at a frequency of 50 kHz. The tissue surrounding the rods exceeded 50°C and confluent tissue necrosis was noted in 7 of 9 (78%) kidneys. Necrosis extended 2 mm beyond the periphery of the rods and there were no 'skip areas' of viable tissue. This application is awaiting human trials.

### **Conclusions**

There have been tremendous strides in the management of small renal tumors. Progress has been made in decreasing the morbidity of procedures and improving the safety and feasibility of minimally invasive approaches. Ablative technologies currently offer the



promise of outpatient, lowmorbidity procedures to manage small tumors without the need for open or laparoscopic surgery. Technologies such as HIFU possess the potential to allow for management of renal tumors without any incision.

At this time, the most extensive experience has been with cryoablation, but is limited primarily to laparoscopic applications. On the other hand, although RFA is increasingly popular and allows percutaneous treatment, physicians have less experience in its use. Long-term cancer control by these modalities has not yet been established, but early results are promising.

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## 36

# Novel therapies for advanced renal cell carcinoma

Stephen E Pautler, Jan Roigas and McClellan M Walther

### Introduction

The incidence of kidney cancer is increasing in the United States,<sup>1,2</sup> with an estimated incidence of 30,800 cases in 2001 with 12,100 deaths.<sup>3</sup> Approximately, one-third of patients presenting with kidney cancer have metastatic disease at presentation,<sup>2</sup> which greatly reduces the ability to cure patients. Surgical resection of the primary tumor and solitary metastases offers a potential cure for only about 20% of patients. Systemic therapies for metastatic kidney cancer have a poor response rate, although a great effort worldwide to improve these outcomes is ongoing. This chapter will discuss the role of cytoreductive laparoscopic radical nephrectomy (LRN) and we will briefly discuss recent advances of systemic therapies in the context of metastatic kidney cancer.

### Diagnosis

The classically described presentation of kidney cancer with gross hematuria, flank pain, and a palpable mass occurs infrequently. Currently, an increasing number of patients are presenting with incidentally discovered renal masses.<sup>4</sup> With a larger use of computer tomography (CT) imaging, a stage migration toward more localized disease has occurred, but 40% of patients still present with metastatic disease. Symptoms attributed to metastatic renal cell carcinoma (RCC) include gross hematuria, flank pain, weight loss, and a variety of paraneoplastic syndromes.

Patients presenting with a solid renal mass suspicious for RCC should undergo a complete history and physical examination. Ancillary investigations include a contrast CT scan of the abdomen/pelvis (Figure 36.1), chest radiograph, blood work (Table 36.1) and urinalysis with urine cytology and/or cystoscopy reserved for cases of possible transitional cell carcinoma. Bone scans are recommended



**Figure 36.1** Computed tomography of left renal tumor. A 30-year-old male underwent cytoreductive laparoscopic radical nephrectomy with morcellation for an 8 cm×8 cm left-sided renal tumor that proved to be renal cell carcinoma. The patient had small volume lung metastases and was placed on a randomized trial of systemic interleukin-2 immunotherapy.

for patients with symptomatic bone pain or elevations in the serum calcium or alkaline phosphatase levels. Chest CT can be performed to better characterize abnormalities on the plain film.<sup>5</sup> Magnetic resonance imaging (MRI) is an excellent modality to delineate renal vein or vena cava involvement with tumor thrombus<sup>6</sup> and is recommended in any questionable cases.

### Treatment options

Treatment options are limited for patients with metastatic RCC. Based on the biological and clinical observations in

**Table 36.1** *The basic work-up for a renal mass that is suspicious for renal cell carcinoma*

Blood work:  
 Complete blood count  
 Coagulation profile  
 Serum electrolytes  
 Alkaline phosphatase

Serum calcium

Transaminases (ALT and AST)

Urine:

Urinalysis

Urinary cytology<sup>a</sup>

Radiographic work-up:

Pre- and post-contrast CT of the abdomen

Chest radiograph

Bone scan<sup>b</sup>

Percutaneous biopsy of renal mass<sup>c</sup>

Cystoscopy<sup>d</sup>

<sup>a</sup>Urine cytology is reserved for instances where transitional cell carcinoma is suspected and all cases of presenting with hematuria.

<sup>b</sup>Bone scan is recommended for patients with elevated serum calcium or symptoms of bone pain.

<sup>c</sup>Percutaneous biopsy of the renal mass is limited to cases where the origin of the tumor is in question, such as multifocal renal tumors, renal lymphoma, or possible metastatic disease from another source.

<sup>d</sup>Cystoscopy is reserved for patients who present with hematuria. ALT=alanine transaminase, AST=aspartate transaminase, CT=computed tomography.

the past, a wide variety of chemotherapeutic, hormonal and immunotherapies have been assessed. Currently, the only Food and Drug Administration (FDA) approved therapy is systemic administration of interleukin-2 (IL-2). Objective responses ranging from 10% to 20% have been seen in various clinical trials.<sup>7,8</sup> A small cohort of patients with advanced RCC at an isolated site of disease is amenable to surgical treatment. In select patients with resection of pulmonary metastases from RCC, for example, a 5-year survival of 35–39% has been found.<sup>9,10</sup>

With respect to novel therapies for advanced RCC, a recent innovation was the concept of laparoscopic cytoreduction prior to administration of systemic immunotherapy. The role of cytoreductive nephrectomy remains somewhat controversial. Clear indications for cytoreductive nephrectomy include the palliation of unmanageable pain attributed to the primary tumor or gross hematuria. Surgery as treatment of paraneoplastic syndromes such as hypercalcemia has had mixed utility in the short term.<sup>11</sup> At the present time, we perform cytoreductive nephrectomy for palliative reasons when indicated. Additionally, we limit elective cytoreductive nephrectomy to patients being treated with systemic immunotherapies in the context of prospective trials.

Other minimally invasive procedures have a limited role in the treatment of advanced kidney cancer. Two techniques that do merit attention are percutaneous embolization and percutaneous radiofrequency ablation (RFA). One of the most widely studied minimally invasive modalities in metastatic RCC is embolization.<sup>12–16</sup> Palliative percutaneous, transvenous embolization is effective for the control of hemorrhage or gross hematuria caused by large renal tumors.<sup>17</sup> With respect to cancer control, embolization with or without surgery has limited success.<sup>12–16</sup> Initial reports of this strategy had encouraging results<sup>15,16</sup> but several other studies revealed less impressive responses and survival rates.<sup>12,13</sup> Embolization in combination with radioactive iodine has been reported with some moderate success.<sup>18</sup> The current role of embolization in advanced kidney cancer appears to be limited to palliative indications. Further study of the role of embolization of



the renal primary will probably occur in the context of the study of other systemic adjuvant therapies.

RFA techniques are currently being developed and studied for the treatment of small primary renal tumors.<sup>19–21</sup> RFA causes coagulative necrosis through molecular friction and heating of the targeted tissue. Short-term outcomes of RFA for small renal tumors have been encouraging, with a 79% success rate.<sup>20</sup> Experience with renal RFA has been limited to smaller tumors (<5 cm) and, thus far, long-term outcomes have not been reported.<sup>19,21</sup> Experience with RFA for renal tumors in advanced RCC is extremely limited. RFA has been utilized after failure of embolization for the control of gross hematuria due to a renal tumor in the setting of metastatic disease and a solitary kidney.<sup>22</sup> The technique was considered a success, although complete tumor ablation has not been attempted. Additionally, RFA has been applied to the treatment of a splenic metastasis of RCC.<sup>23</sup> The role of RFA in this context remains to be defined.

### **Indications and contraindications for cytoreductive laparoscopic radical nephrectomy**

Palliative indications for cytoreductive nephrectomy include gross hematuria causing shock or requiring repeated blood transfusions, irretractable pain due to local invasion or compression by the primary tumor, and paraneoplastic syndromes in selected patients.<sup>24</sup> Cytoreductive nephrectomy prior to the administration of systemic immunotherapies is a relative indication. Results of immunotherapy trials in which cytoreduction was not performed are extremely poor, with rare responses seen in the primary renal tumor.<sup>25</sup>

Specific contraindications to cytoreductive LRN include level III vena cava tumor thrombus, extensive contiguous organ extension precluding laparoscopic resection and poor performance status of the patient. Relative contraindications include pregnancy, uncorrected coagulopathies, brain metastases, and extreme obesity. With increasing laparoscopic experience, vascular techniques have evolved to the point where level I-II vena caval thrombi have been resected successfully.<sup>26,27</sup> Additionally, diaphragm invasion, splenic and distal pancreatic involvement do not contraindicate a laparoscopic approach if the surgeon is experienced with the advanced laparoscopic techniques required to complete these procedures.<sup>28</sup> Difficult LRN are demanding procedures and should be performed by experienced urologic laparoscopists.

### *Patient and preoperative preparation*

Preoperatively, patients undergo a mechanical/antibiotic bowel prep and are hydrated overnight with intravenous fluids. Generally, a first-generation cephalosporin antibiotic is administered prophylactically. For deep venous thrombosis prophylaxis, patients receive subcutaneous heparin and pneumatic stockings are utilized during the operation. Central venous and arterial line monitoring are essential, as the blood loss encountered during cytoreductive LRN can exceed LRN for localized kidney cancer. A Foley catheter is placed. We utilize an orogastric tube for stomach decompression and inhaled nitrous anesthesia is avoided. Patients are positioned with the ipsilateral flank up, the ipsilateral arm supported by a Kraske arm board, and all pressure points are padded (Figure 36.2).



**Figure 36.2** Patient positioning for a left laparoscopic radical nephrectomy. Careful padding of all pressure points is mandatory to prevent postoperative complications.

#### *Recommended equipment and instruments*

Standard laparoscopic equipment is used for cytoreductive LRN (Table 36.2). Particularly useful tools include the harmonic scalpel and endoshears. An endovascular stapling device is used for control of the renal artery and vein in separate firings of the instrument. For cytoreductive LRN, specimen removal by morcellation is an attractive option to decrease the morbidity associated with intact extraction. The risk of port-site recurrence in this patient population is unknown but such an event is not likely to have a profound impact on patient survival. In cases where morcellation is performed, an impermeable sac such as the LapSac (Cook Urological, Spencer, Indiana) is recommended. Metastases related to tumor morcellation are extremely rare. Laparoscopic ultrasonography is a useful adjunct for the intraoperative assessment of the renal vein and should be available.

#### **Approach and tips**

The transperitoneal approach is recommended for the majority of cytoreductive LRN with access achieved by

**Table 36.2** *Instruments recommended for use in a cytoreductive laparoscopic radical nephrectomy*

Necessary equipment:  
 Hasson cannula  
 0° laparoscope  
 30° laparoscope  
 12 mm trocar (×3)  
 5 mm trocar (×2)  
 10 mm right-angle dissector

Maryland dissector  
 Endoshears  
 5 mm harmonic scalpel  
 10 mm clip applier  
 Endovascular stapler  
 Suction-irrigator  
 10 mm fan retractor  
 10 mm spoon forceps  
 Optional equipment:  
 5 mm 0° laparoscope  
 Laparoscopic ultrasound probe  
 5 mm clip applier  
 LapSac<sup>a</sup>  
 Tissue morcellator  
 Sponge forceps  
 5 mm atraumatic locking grasping forceps (×3)  
 Carter-Thomason port closure kit  
<sup>a</sup>Lapsac (Cook Urological, Spencer, Indiana).

Hasson technique. In many patients, the primary renal tumor for cytoreduction is quite bulky (>10 cm), leading to possible distortion of the normal anatomic landmarks. The open access technique allows controlled access to the abdomen without the possibility of a Veress needle injury to the primary tumor or displaced intra-abdominal viscera. As previously reported, no difference in bowel injuries was seen between the open (Hasson) or closed (Veress) techniques in several studies,<sup>29–31</sup> although these access techniques have not been studied prospectively in the cytoreductive LRN patient population. The transperitoneal approach yields the largest working area and allows the surgeon to identify familiar structures. We have reserved the retroperitoneal approach for a subset of



**Figure 36.3** The peritoneal attachments of the colon are incised at

the 'white' line of Toldt to expose Gerota's fascia.



**Figure 36.4** To further expose Gerota's fascia and the tumor, the colon mesentery is separated from Gerota's fascia by incising the colorectal ligament.

patients with small renal primaries and no evidence of lymphadenopathy or local invasion as seen on preoperative imaging.

The steps of the procedure follow those of a standard LRN for localized disease, as made popular by Clayman and colleagues.<sup>32</sup> Briefly, the bowel is mobilized off the retroperitoneum and kidney (Figures 36.3 and 36.4). For right-sided tumors, liver retraction is important to give access to the upper pole and adrenal gland (Figures 36.5–36.7). Dissection onto the vena cava is performed and the renal vein is identified. Subsequent dissection of the upper pole and ligation of the adrenal vein is performed. Next, the ureter is identified and the lower pole mobilized and elevated to facilitate access to the hilum. With



**Figure 36.5** The peritoneal reflection is incised under the liver.



**Figure 36.6** The peritoneal reflection is incised under the liver.

particularly large tumors, retraction using 5 mm instruments is difficult and in these situations a spoon forceps allows enough purchase to effectively retract the kidney. The renal artery is controlled with clips or an endovascular stapler. We advocate close inspection of the renal vein to ensure that it collapses, suggesting no secondary arterial blood flow (Figure 36.8). The renal vein is routinely ligated using an endovascular stapler (Figure 36.9). Following ligation of the ureter, the remainder of the kidney is mobilized and the specimen removed by morcellation or intact extraction (Figure 36.10). For left-sided tumors, the bowel is mobilized; the gonadal vein is identified and followed to the hilum. Other important differences include the ligation



**Figure 36.7** The peritoneal reflection is dissected away from the upper pole of Gerota's fascia.



**Figure 36.8** The renal vessels are exposed by upward retraction of the ureter at the lower pole. The renal artery is secured first with a vascular GIA stapler.

of the adrenal and lumbar veins and gentle handling of the tail of the pancreas if it is encountered during dissection. Mobilization of the lateral attachments of the spleen to the abdominal wall allows the spleen to fall medially and out of the dissection field, similar to the dissection performed during laparoscopic adrenalectomy.<sup>33</sup>

Recently, Moore et al described operative techniques to assist in controlling parasitic tumor blood vessels for primary renal lesions greater than 8 cm in size.<sup>34</sup> With this approach, the renal unit is mobilized before securing the renal vessels. A vascular Endo-GIA stapler (US Surgical, Norwalk, Connecticut) is used to control all attachments to Gerotas fascia (Figure 36.11). This technique has

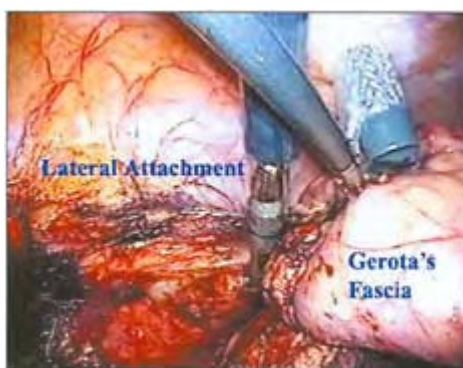


**Figure 36.9** The right renal vein (RV) is ligated using an endovascular stapler. During cytoreductive LRN,

bulky lymph nodes can obscure the renal hilum, mandating meticulous dissection of the vessels prior to ligation.



**Figure 36.10** The tumor specimen is entrapped with an Endo Catch II device and extracted through an extended umbilical incision.



**Figure 36.11** All parasitic vessels and attachments to Gerota's fascia are secured by vascular GIA staplers.

demonstrated a decrease in blood loss compared with open cytoreductive nephrectomy series and other laparoscopic series.<sup>35-45</sup>

In cases in which a level I renal vein thrombus is known or suspected, laparoscopic sonography can be employed to confirm the distal extent of the thrombus and the blood

flow. In situations where the renal artery has been secured and flow in the renal vein has not decreased, the laparoscopic ultrasound probe in Doppler mode can be used to identify secondary arteries or aberrant vessels.

Extensive dissection of intra-abdominal disease is possible through a laparoscopic approach. Ipsilateral lymphadenectomy is routinely performed for visible disease. Careful hemostasis and judicious use of clips is recommended to prevent unnecessary bleeding or postoperative lymphocele formation. For tumors that are invasive into the diaphragm, resection is possible with the use of the harmonic scalpel. Defects in the diaphragm generally require suture repair, and chest tube placement is recommended at the completion of the operation to prevent hemothorax.<sup>28</sup> The patient must be monitored for hypercarbia or other signs of cardiorespiratory compromise during a diaphragm resection. In unstable patients, urgent chest tube placement or conversion to open is performed. Laparoscopic resection of the spleen and/or the tail of the pancreas can be performed when indicated. The endovascular-stapling device is useful for controlling the splenic hilum, short gastric vessels, and for coming across the pancreatic parenchyma. There are reports of misfiring staplers and urgent control of hemorrhage is mandatory.<sup>35</sup> Urologists must be aware of this possibility and should be prepared in the event that this occurs. If conversion is required, the two subcostal working ports are connected using a scalpel. Rapid control of the hilum is obtained using this approach.

### *Complications*

Open cytoreductive nephrectomy is associated with significant complication rates, ranging from 13 to 50%.<sup>36-40</sup> Laparoscopic cytoreduction appears comparable with respect to the incidence and type of complications. The complications of cytoreductive LRN are similar to those of LRN for localized disease. Several important differences require discussion. First, due to the advanced nature of the kidney cancer, the average blood loss during cytoreductive LRN is greater than that encountered during procedures for localized cancers. Bulky lymphadenopathy and parasitic tumor vessels can contribute to the increased bleeding observed. Cytoreductive LRN can lead to skin blistering and contralateral psoas necrosis due to the prolonged operating times with the patients in the flank position. Preventive measures such as not using a beanbag or kidney rest during patient positioning reduces these problems. Unresectability of a kidney tumor can occur with extensive involvement of the duodenum, head of the pancreas, common bile duct, or great vessels. These situations are not always predicted by preoperative imaging.

### *Results*

The current treatment of metastatic RCC is changing with advances in the fields of immunotherapy, gene therapy, and chemotherapy. The role of cytoreductive surgery in the treatment algorithm is also evolving. Several issues surrounding debulking surgery for kidney cancer merit discussion. Historically, a large percentage of patients who underwent cytoreduction were unfit to receive systemic immunotherapy postoperatively for various reasons, such as progressive disease, postoperative complications, and declining performance status.<sup>39,40</sup> In the recent experience of the National Cancer Institute, 38% of patients who underwent open cytoreduction did not receive systemic



high-dose IL-2.<sup>7</sup> The mortality rate from open cytoreductive nephrectomy ranges up to 4%.<sup>24</sup> The rationale for cytoreduction has been based on several observations. First, primary tumors rarely respond to systemic immunotherapy and, with removal, the greatest chance of response is afforded to the patient and the major source of further metastases is eliminated. Additionally, patients may have less pulmonary toxicity as a result of IL-2 administration postoperatively.<sup>40,41</sup> Two recently published prospective randomized trials identified a survival advantage of 3–10 months for patients who underwent open cytoreduction followed by interferon-alpha 2b (IFN- $\alpha$ 2) administration in comparison to those who received IFN- $\alpha$ 2 alone.<sup>42,43</sup> The reason for the survival advantage is not obvious, as both arms had the same response rate to the systemic therapy and the nephrectomy arm had a slight performance status advantage relative to the control arm.<sup>44</sup> Although the clinical significance of the observed survival advantage is unclear, these studies provide the basis for further investigation into the role of cytoreductive nephrectomy in randomized prospective controlled trials.

To date, limited results are available for cytoreductive LRN. In a pilot study, Walther et al demonstrated the feasibility of the procedure.<sup>45</sup> The goal of minimally invasive surgery is the reduction of morbidity while providing similar surgical outcomes as open surgery. The results of the cytoreductive LRN pilot project support this concept. Advantages were seen for the pure laparoscopic approach with specimen morcellation. Patients required less postoperative narcotics, a shorter hospital stay, and had a shorter recovery time to be fit for the administration of systemic IL-2 therapy. In this initial experience, blood loss was higher than reported for LRN in localized disease,<sup>45,46</sup> probably reflecting the difficulty of the procedure with findings such as bulky lymphadenopathy, local invasion, and large tumors. Operative times for cytoreductive LRN were significantly longer when compared to open cy to reduction.

Specimen removal during LRN remains a somewhat controversial subject. The arguments against morcellation include the risk of port-site seeding and the lack of accurate pathologic staging. Port-site metastases have rarely been reported with localized kidney cancer<sup>47,48</sup> but not in the cytoreductive setting. Additionally, patients with advanced RCC have other documented metastases that require the administration of systemic therapy and portsite seeding would not be a catastrophic event. Histologic confirmation of RCC in advanced disease is important prior to pursuing systemic immunotherapy, whereas staging information does not alter patient management. Evidence exists that accurate histologic diagnosis is possible from morcellated kidney tumors in both the localized<sup>26,49–51</sup> and cytoreductive setting.<sup>52</sup>

## Conclusion

Early experience with cytoreductive LRN for advanced RCC has been encouraging. These cases can be difficult and can require a broad range of ablative laparoscopic techniques. Further prospective multi-institutional studies of laparoscopic cytoreduction are required to define the role of this procedure in the care of this devastating disease.

## Treatment of advanced renal cell carcinoma

About one-third of patients diagnosed with RCC have metastatic disease at the time of first presentation and another 20–30% will develop metastases during further follow-up. For these patients therapeutic options are limited and cure from cancer is a rarity. It is a common observation that metastatic RCC does not respond to conventional therapies such as chemotherapy, hormonal therapy, or radiation therapy. However, since the clinical implementation of immunotherapy, progress has been made and, together with malignant melanoma, metastatic RCC is a classic example of a disease which can at least, partially, be managed with immunomodulatory treatment strategies.

Several recent studies have provided evidence for a treatment approach in patients with metastatic RCC that combines the operation on the primary tumor and the subsequent immunotherapy for treatment of unresectable metastases.<sup>42,43</sup> Currently, there is no therapeutic standard defined for the immunomodulatory treatment of metastatic RCC. Therapeutic strategies are still in the experimental phase and include the unspecific activation of the immune system on the basis of cytokines such as IL-2 or IFN- $\alpha$ 2, specific vaccination approaches, and adoptive immunotherapeutic concepts. Thus, treatment of metastatic RCC is often performed in phase I or II studies. There is only limited clinical experience from phase III studies, providing information on the efficacy of different treatment schedules and long-term survival data. Also, the performance of studies with a 'no treatment' arm remains unacceptable from the ethical point of view. Thus, to date, the treatment of metastatic RCC is still an experimental approach but it offers the great chance of identifying new, innovative, and effective therapeutic strategies.

### *Cytokine treatment*

The cytokines IL-2 and IFN- $\alpha$ 2 play an important role in the treatment of metastatic RCC. IL-2 was clinically introduced by Rosenberg in 1985 and has been approved by the FDA.<sup>52</sup> With the intravenous application of IL-2, response rates of 15% have been reported, with an estimated longterm survival of 10–20% after 5 and 10 years.<sup>53</sup> One of the problems of high-dose intravenous application of IL-2 is the degree of side-effects, which require hospitalization of the patients.

The combination of IL-2 and IFN- $\alpha$ 2 has been prospectively analyzed in the CRECY study (Cancer du Rein Etude Cytokine) in 1996 on 425 patients.<sup>54</sup> Although the combination of the cytokines resulted in a significantly enhanced response rate and duration of the progression-free survival, mean survival was not significantly different (IFN- $\alpha$ 2, 13 months; IL-2, 12 months; and IFN- $\alpha$ 2+IL-2, 17 months;  $p=0.55$ ).

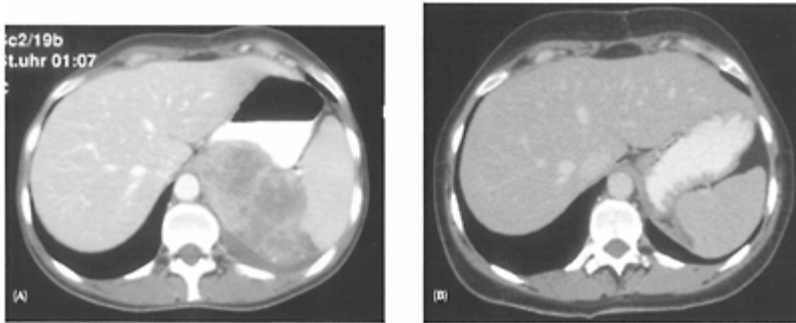
Considering the side-effects of intravenous IL-2, efforts have been made to reduce toxicity by subcutaneous application of IL-2. In a multi-institutional trial on 152 patients, Atzpodien and coworkers reported a 25% response rate with subcutaneous IL-2 in combination with IFN- $\alpha$ 2.<sup>55</sup>

On the basis of preclinical data, the cytokines IL-2 and IFN- $\alpha$ 2 have been further combined with the pyrimidine antagonist 5-fluorouracil (5-FU). Recently, Atzpodien and

coworkers have published their results of a prospective randomized trial comparing immunochemotherapy using subcutaneous IL-2, subcutaneous IFN- $\alpha$ 2 and intravenous 5-FU with tamoxifen. Here, in 41 patients treated with immunochemotherapy, median survival was 24 months with a 5-year survival rate of 24.8% compared with 13 months and 13.5% in the tamoxifen-treated control group.<sup>56</sup> The results of the immunochemotherapeutic regimen discussed are controversial. In the studies of Negrier et al<sup>57</sup> and Ravaud et al<sup>58</sup> low rates of objective remissions were observed. In a multicenter phase III study with 131 patients, the effects of 5-FU were tested by comparing IL-2 and IFN- $\alpha$  vs IL-2, IFN- $\alpha$ , and 5-FU. No complete responses were observed and only 5 partial responses in the triple drug arm.<sup>56</sup> In the multicenter phase II study of Ravaud on 105 assessable patients, objective remissions occurred in only 1.8%.<sup>58</sup> However, it has to be considered that, in both trials, a treatment protocol was used with a lower cumulative dose of the cytokines combined with a higher cumulative dose of 5-FU compared with the original subcutaneous treatment schedule.

Another treatment option for patients specifically suffering from pulmonary metastases of RCC is the inhalative application of IL-2, which was first reported by Huland and coworkers. With the inhalative approach, response rates of up to 15% and stabilizations of another 55% of patients, with the advantage of a reduced toxicity compared with intravenous IL-2, have been reported.<sup>59,60</sup> However, a prospective randomized trial comparing the inhalative treatment with intravenous or subcutaneous application of IL-2 has not yet been performed. The inhalative IL-2 approach is cost-intensive and requires a high patient compliance.

Recent efforts focus on the further clinical improvement of immunotherapy. The rationale of a combination of immunotherapy and local radiation has been tested *in vitro* using the RENCA murine renal carcinoma model.<sup>61,62</sup> Taken together, these studies have demonstrated an enhanced therapeutic efficacy of the combined treatment, resulting in a reduced number of pulmonary metastases, the reduction of primary tumor size, and an increased survival. Brinkmann and coworkers have demonstrated in an initial report that the simultaneous application of radiation therapy and immunochemotherapy might result in a high rate of objective remissions in patients suffering from symptomatic bone or lymph node metastases or local recurrences.<sup>63</sup> Of 12 patients, 9 with bone metastases and 3 with local recurrences were locally irradiated. Complete remissions were reached in 4 patients (33%) and partial remissions in another patient (8%), which was a high rate when compared to results with immunotherapy alone. Only 4 patients (33%) remained progressive under combined therapy. After a median follow-up of 28 months, 75% of the patients were still alive. All patients had subjective pain relief after 2 weeks of treatment. Figure 36.12A and B are CT scans of a 35-year-old female patient with a



**Figure 36.12** (A and B) A 35 year old female patient with a left clear cell renal carcinoma following R2 resection (pT3a pN2 G2) and subsequent progression of retroperitoneal lymph node metastases. The patient received 3 cycles of immunochemotherapy combined with local radiation therapy of the left retroperitoneal masses. A complete response was achieved. The patient has NED after a follow-up of 34 months (left side: CT scan prior to therapy, right side: CT scan after 3 cycles of immunochemotherapy and radiation therapy).

left clear cell renal carcinoma following cytoreductive nephrectomy resection (pT3a pN2 G2) and subsequent progression of retroperitoneal lymph node metastases. After 3 cycles of immunochemotherapy combined with local radiotherapy, complete remission was achieved.

#### *Vaccination therapy*

In contrast to the cytokine treatment, most vaccination approaches aim at the development of a specific antitumor immune response. Principally, the lysis of tumor cells depends on the binding of immunologic effector cells (such as CD8<sup>+</sup> cytolytic T lymphocytes) on tumor-associated antigens which are presented on the surface of the tumor cell. Vaccines contain the information of specific known or unknown tumor-associated antigens which can be mediated via native or modified intact tumor cells, tumor cell lysates, or defined fragments from tumor cells (peptides). The development of an immune response further depends on the presentation of antigens via professional

antigen-presenting cells such as dendritic cells and costimulatory signals which are antigen independent and serve for the activation of immune effector cells. Therefore, current vaccination strategies include the use of native or modified tumor cells, tumor cell lysates, isolated immunogenic peptides, or in-vitro pulsed dendritic cells. Although there are a large variety of different vaccination concepts, only a limited number of phase I/II trials have shown clinical efficacy of vaccines in the treatment of metastatic RCC.

Kugler and coworkers reported on 17 patients treated with a hybrid cell vaccine generated via electrofusion of allogeneous tumor cells and autologous dendritic cells.<sup>64</sup> Fused cells represented tumor-associated antigens as well as costimulating capabilities of dendritic cells. After a mean follow-up of 13 months, 4 complete remissions (23.5%) and 2 partial remissions (11.8%) were observed. This study provided evidence for the clinical efficacy of an individualized immune therapeutic approach based on the induction of cytolytic T lymphocytes against multiple and different tumor-associated antigens.

In another study, 37 patients were treated with pulsed dendritic cells either loaded with autologous tumor cell lysate or with the lysate of the renal cancer cell line A-498 and with the addition of keyhole limpet hemocyanin.<sup>65</sup> After a mean follow-up of 24.6 months and 29 evaluable patients, 2 complete and 1 partial remissions were seen. Remissions occurred only in patients treated with dendritic cells pulsed with autologous tumor cell lysate. Both studies mentioned refer to the potential capability of dendritic cell-based vaccines for inducing a specific immune response leading to tumor regression in metastatic RCC.

Another concept for vaccination is the use of heat shock proteins associated with tumor-derived peptides eliciting antigen-specific cytolytic T lymphocytes. Heat shock proteins serve as molecular chaperones for tightly bound cellular peptides that are believed to represent a cellular repertoire of immunogens. Using an autologous heat shock protein-peptide vaccine 1 complete and 3 partial remissions were observed in 29 patients with metastatic RCC.<sup>66</sup> Heat shock protein-based vaccines will be further investigated, either in combination with a variety of known immunogenic peptides, cytokines, or dendritic cells.

### *Adoptive immunotherapy*

Because of the immunogenic properties of RCC and its susceptibility to immunotherapy, an innovative therapeutic approach is nonmyeloablative allogeneic stem cell transplantation, first reported for metastatic RCC by Childs and coworkers in 2000.<sup>67</sup> This therapeutic strategy aims, in the same way as observed in hematologic cancers, at the development of a graft-vs-tumor effect, which can lead to the regression of metastases. In the abovementioned study only stem cell allografts from an HLA-identical sibling or a sibling with one mismatch of an antigen were transplanted. The graft-vs-tumor effect strongly correlated with the occurrence of a complete donor-T-cell chimerism and the development of a graft-vs-host disease. After a median follow-up of 402 days in 19 treated patients, 10 objective remissions (53%) were observed, with regression occurring in different metastatic sites such as lymph nodes, subcutaneous metastases, or liver and bone metastases. However, stem cell transplantation was associated with a 12% mortality rate (2 patients died due to severe graft-vs-host disease or bacterial sepsis).

Taken together, the stem cell transplantation technique offers an interesting therapeutic concept for selected patients which needs to be further evaluated in multicenter clinical trials.

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## Minimally invasive treatments for bladder cancer—from transurethral resection to laparoscopic radical cystectomy

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### Introduction

#### *Overview of bladder cancer presentation*

De-novo bladder cancer most commonly presents with gross or microscopic hematuria. As cystoscopy is a mandatory part of any complete work-up for hematuria, this is the most common test that confirms the diagnosis. Bladder cancers may also create filling defects that are visible on an intravenous pyelogram (IVP), ultrasound, and/or computed tomography (CT) scan. However, sensitivity is poor when tumors are less than 2 cm, and therefore incidental detection of bladder cancer is unusual.

Currently there is no commonly accepted screening test for bladder cancer, other than urinalysis to detect microscopic hematuria. Cytology has been used to detect preclinical cancer in high-risk populations, i.e. those subjects involved in chemical industrial exposure. Again, cystoscopy provides visual confirmation and the avenue for securing tissue for histopathology. Interval cystoscopy is also indicated for individuals with a history of bladder cancer or a history of upper tract transitional cell carcinoma. Another high-risk group includes those with a chronic suprapubic catheter where a transitional or squamous transitional or pure squamous cancer occurs with increased frequency. They should undergo yearly cystoscopy and cytology studies. For individuals with a history of bladder cancer undergoing routine cystoscopy, urinary cytology is an adjunct surveillance study that is standard. Cytology is sensitive for carcinoma-in-situ and high-grade transitional cell carcinoma, but notoriously insensitive for detecting low-grade tumors. Several urinary marker tests such as BTA and NMP-22 have been investigated that are more sensitive in detecting low-grade tumors, but none have such accuracy that cystoscopy can be safely omitted in the face of normal urine marker tests. Thus, the use of newer urine markers has yet to become standard, and the standard of care remains cystoscopy to detect papillary tumors of all grades, and cytology to assist with the diagnosis of carcinoma-in-situ and high-grade invasive recurrence, and to alert for possible upper tract tumor occurrence.

*Physical examination*

A complete history and physical examination is an important part of any evaluation of bladder cancer. As transurethral resection (TUR) is the mainstay of initial diagnosis and treatment, patients must be judged safe to undergo a general anesthetic. Patients with bladder cancer often have a significant smoking history, and must therefore be screened for other smoking-related conditions such as coronary artery disease, peripheral vascular disease, lung cancer, emphysema, and chronic obstructive pulmonary disease. A complete genitourinary examination surveys for the presence of other conditions such as prostate cancer, urethral masses, and in females any adnexal masses.

The most important part of the physical examination specific to bladder cancer is the pelvic examination under anesthesia before and at the conclusion of the TUR. The physician should perform bimanual examination with one hand on the abdomen and an examining finger in the rectum (males) or vagina. With the patient maximally relaxed by the anesthesiologist, the bladder walls are compressed between the examining hand and finger and systematically palpated laterally and medially. Again, patient muscular relaxation is critical to being able to adequately feel for bladder masses. Optimally, the examination should be repeated with the opposite hand on the abdomen/finger in the rectum or vagina. Any induration or two-dimensional mass that persists after the tumor resection may represent unresected tumor more deeply invasive in a primary case, or possibly scar in a patient after a recent transurethral resection of bladder tumor (TURBT). A three-dimensional mass is highly indicative of a locally advanced muscle invasive tumor.

*Diagnostic work-up and staging*

Given that bladder cancer is commonly related to smoking and occurs in older individuals, diagnostic work-up will turn towards appropriate preparation for transurethral resection. Complete blood counts, electrolytes, chest X-ray, and electrocardiogram (ECG) are obtained and possible medical/cardiac clearance in appropriate patients. While spinal anesthesia is an option, many prefer a general anesthetic so that the patient can be maximally relaxed with muscular paralytic agents for bimanual examination, and avoid an obturator reflex during lateral resection. When histopathology reveals high-risk superficial disease or muscle invasive disease, further staging for metastatic disease is done with a CT of the abdomen and pelvis, and serum liver function tests. A chest CT is obtained for any suspicious chest X-ray finding, and nuclear bone scans are obtained if alkaline phosphatase is elevated or if the patient complains of bone pains (excluding chronic conditions).

**Transurethral technique**

While TURBT is a routine procedure for urologists, many surgical goals require careful attention to detail and technique. Pre-existing urinary infections are treated before surgery and uninfected patients are given prophylactic antibiotics. In general, TURBT is a low-

risk procedure with few major complications or mortalities. Patients are advised of the risks of bleeding and bladder perforation. The aim of resection is complete removal of visible cancer and harvest of tissue for accurate staging, while controlling bleeding and avoiding perforation. While not technically ‘complications,’ several untoward outcomes occur after TURBT. First and foremost, bladder tumors recur, regardless of initial grade and stage. A field defect and tumor cell reimplantation are certainly among the causes, while other causes are missed or inadequately resected tumors. Pathologic examination of the specimens may also identify problems with the technique of resection that prevents ideal characterization and management. The two most common problems are excessive cautery artifact in the specimen and a lack of muscularis propria in the specimen. When either of these situations occurs in the setting of a high-grade lesion, the urologist cannot reliably stage the patient as superficial vs muscle invasive, and reresection becomes mandatory. At the other extreme, excessively deep resection may lead to bladder perforation, which may, in theory, allow tumor cells to implant in the pelvis, and which necessitates additional catheter time to heal the injury. Furthermore, perforation along the posterior wall of the bladder may penetrate the intraperitoneal abdominal cavity and require open or laparoscopic repair.

With these issues in mind, the technique of TURBT starts with equipment. A full range of resectoscopes and dilators are needed to negotiate the urethra safely with minimal trauma, thereby avoiding postoperative stricture formation. The use of continuous flow is popular with some urologists and may aid in visualization with bleeding, prevents the need for repetitive interruption to drain the bladder, and keeps the bladder wall in a relatively ‘stable’ position of distention throughout resection. Complete inspection of the bladder is best achieved with use of a 12° or 30° lens and a 70° lens. Inspection at different filling levels and with manual suprapubic pressure helps visualize the more acute angles of view along the anterior walls and bladder neck. Photographs and/or bladder maps help document the number, location, and size of tumors for future reference.

The technique of resection varies with the size and location of the tumor. Small, papillary lesions may often be removed by a cold-cup biopsy grasper alone. Larger tumors require a standard resectoscope loop using cutting current to preserve tissue for pathology. When more aggressive pathology is suspected, the tumor specimen should be fractionated into superficial and deep layers. The deeper layers should include resected muscularis propria under the tumor, and possibly cold-cup biopsies of the area to exclude invasive disease. With higher-risk tumors, random bladder biopsies and prostate urethral biopsies are obtained to identify surrounding carcinoma-in-situ and/or prostatic urethral involvement.

Post-procedure, a large catheter is placed, and the duration varies depending on the difficulty and depth of resection performed. Evidence is now available that a single post-TURBT instillation of a chemotherapeutic agent such as mitomycin C or Adriamycin (doxorubicin) will help reduce recurrences with minimal morbidity. Routine use is incorporated in the European Association of Urology Guidelines on Bladder Cancer (download from their website [www.uroweb.org](http://www.uroweb.org)), and can now be recommended unless perforation occurred—even when further therapy with BCG (bacille Calmette-Guérin) is anticipated.<sup>1,2</sup>

### Transurethral outcome

Outcomes after transurethral resection for superficial pTa or pT1 tumors are measured in terms of tumor recurrence and tumor progression. Both outcomes are predicted by tumor stage, grade, presence of carcinoma-in-situ, initial tumor size, and multiplicity.<sup>3</sup> Allard et al<sup>4</sup> evaluated adverse predictors of recurrence, including tumor multiplicity, diameter >3 cm, stage T1, and grade 2–3. They reported a strong relationship between the number of adverse predictors and subsequent recurrence/progression. For patients without adverse predictors, recurrence-free survival was 86% at 1 and 69% at 2 years; no patients progressed. For 3–4 adverse predictors, recurrence-free survival was 30% at 1 and 19% at 2 years; 7% of patients progressed.<sup>4</sup> Parmer et al<sup>5</sup> demonstrated the adverse prognostic significance of tumor recurrence at the initial 3-month surveillance cystoscopy. As stated, a single intravesical dose of chemotherapy after resection as well as an induction course can reduce recurrences but not alter progressions.<sup>1,6</sup>

If histopathology from TURBT shows high-risk features for recurrence/progression, i.e. grade 3, stage T1,  $\pm$ presence of carcinoma-in-situ, intravesical therapy with BCG becomes standard. Long-term data are emerging that support durable disease-free survival in most patients, yet approximately 20–30% of patients will progress to muscle invasive disease, and approximately 15% will develop upper tract recurrences.<sup>7,8</sup> Lifelong surveillance is critical, and early cystectomy for patients progressing or recurring with high-risk disease. Maintenance BCG has been shown to reduce recurrences and lengthen worsening-free survival in patients with carcinoma-in-situ and select patients with high-risk Ta/T1 disease,<sup>9</sup> and should be considered in patients who can tolerate the treatment. Newer treatment strategies are also available for patients not tolerating or failing BCG, which combines lower doses of BCG with interferon (IFN). O'Donnell reported efficacy in 40 patients previously deemed BCG refractory, and this finding held true in patients failing one or two 6-dose inductions of BCG.<sup>10</sup> At the very least, BCG/IFN allows for the reduction in dose of BCG for patients with significant symptoms on full dose, and the combination immune response may be superior.

In sum, TURBT is the starting point for all treatments for bladder cancer, and for superficial disease is the mainstay of bladder-sparing treatment. However, as stated, patients with high-risk disease can progress despite therapy, while others have a durable response. Thus, patients can be undertreated if they undergo repeated TURBTs and intravesical therapy, but later progress to invasive disease and are at significant risk for dying of metastatic disease. On the other hand, immediate cystectomy is overtreatment in the majority of T1G3 tumors. The benefits of bladder preservation must be balanced with long-term cancer control. The pendulum may be swinging in favor of earlier cystectomy in cases of BCG failures. Herr and Sogani reported on 307 patients with high-risk transitional cell carcinoma who underwent cystectomy during follow-up after initial BCG and found improved long-term survival when cystectomy was performed early (<2 years) vs late.<sup>11</sup> Solsona et al<sup>12</sup> found that the 3-month response to intravesical therapy predicted for progression-T1G3 recurrences at 3 months after induction BCG had a 66% 1-year and 96% 2-year progression rate. Molecular markers are urgently needed to predict which patients will respond to TURBT plus BCG, and which patients are better served with early cystectomy. Examples of such research include the report from Bernardini et al, who evaluated combining T1 microstaging and p53 expression.<sup>13</sup>

### **Bladder-sparing strategies for muscle invasive disease: transurethral resection of bladder tumor, trimodal therapy, partial cystectomy**

Cystectomy is the gold standard for muscle invasive disease, and as reviewed, is indicated for high-risk superficial disease failing intravesical therapy. For patients presenting with limited muscle invasive disease, TUR alone can be effective. Herr has reported a series of patients treated by TUR alone if re-resection showed pT0 or pT1 residual disease. For pT0, 10-year survival was similar to immediate cystectomy.<sup>14</sup> Solsona et al<sup>15</sup> have reported similar success with select patients with invasive transitional cell carcinoma treated by aggressive TUR alone.

Trimodal therapy has been evaluated as a bladder-sparing treatment for muscle invasive disease: deep TUR, cisplatin-based chemotherapy, and external beam radiation. In their most recent update, Shipley et al<sup>16</sup> reported cancer-specific survival by pathologic stage that was comparable to radical cystectomy at 5 and 10 years: pT2, 74%/66%; pT3-T4a, 53%/52%. The findings of an initial complete resection, absence of hydronephrosis, and no evidence of cancer on restaging resection after 4000 rad selects patients most likely to respond to the chemoradiation regimen. Of note, one-third of patients eventually required a cystectomy, but none for bladder morbidity alone. Thus, trimodal therapy is a valid bladder-preserving option in patients refusing or inappropriate for cystectomy. The extent to which all three treatments are needed is unclear, however, as neoadjuvant cisplatin chemotherapy and TUR is known to produce a PO response at cystectomy<sup>17</sup> and aggressive TUR alone can be successful.<sup>14</sup>

A more invasive, but bladder-spar ing treatment strategy is partial cystectomy. As reviewed by Feneley and Schoenberg,<sup>18</sup> partial cystectomy is feasible but has strict selection criteria that limit its use. The ideal candidate has a solitary lesion located in the dome or anterior wall, well away from the bladder neck and/or trigone. Contraindications include multifocal disease, prostatic involvement, and carcinoma-in-situ. Pelvic lymph node dissection may be performed, and outcomes by stage may match radical cystectomy. However, local recurrence rates of 30–80% have been reported.<sup>18</sup> Other applications of this technique are for tumors arising in diverticula (TUR alone are often inadequate), and adenocarcinoma of the urachus.<sup>18</sup>

### **Laparoscopic radical cystectomy**

Radical cystectomy with urinary diversion remains the gold standard treatment for muscle invasive bladder carcinoma. Constant advances in anesthesiology and surgical technique, and a more sophisticated postoperative care, have decreased the risk of such major surgery. However, radical cystectomy remains an aggressive procedure, with significant morbidity and mortality. The complication rate in the early postoperative period after radical cystectomy and urinary diversion is still 25–35%.<sup>19</sup> This remaining morbidity of open cystectomy has stimulated interest in treatment alternatives with less morbidity without compromising the oncologic outcome.

Advances in laparoscopic surgery have resulted in a notable decrease in patient morbidity, with speedier recovery and shorter hospital stay. Since the first report of a laparoscopic nephrectomy by Clayman and coworkers in 1991,<sup>20</sup> the role of laparoscopy

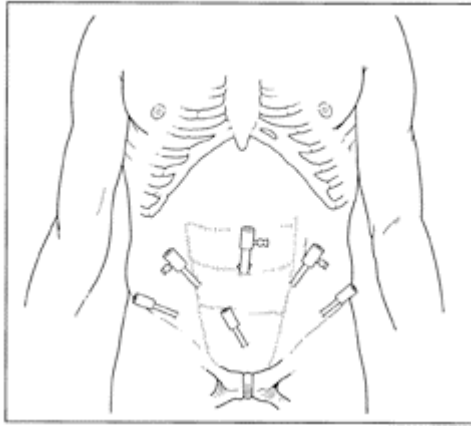
in urology has been expanding. Laparoscopic radical nephrectomy has been established in the last 5 years, with reports of equivalent oncologic results, and the traditional benefits of less postoperative pain, improved cosmesis, shorter hospital stay, and faster return to full activity.<sup>21,22</sup> Recently, laparoscopic radical prostatectomy seems to be as efficacious as the open procedure. Early oncologic data look similar to open series, but only short-term observation is available. However, new benefits are evident with the laparoscopic approach: improved visualization of the operative field with more surgical precision, and significantly lower blood loss.<sup>23–25</sup>

The next logical step is the utilization of the laparoscopic approach for the surgical treatment of muscle invasive bladder cancer. Application of laparoscopy in the field of cystectomy started in 1992 when Parra et al<sup>26</sup> reported a laparoscopic simple cystectomy in a 27-year-old female with symptomatic pyocystitis of a retained bladder after previous urinary diversion. The operating time was 130 min, the blood loss was 115 ml, and the hospital stay was 5 days. In 1993, De Badajoz et al were the first to use the laparoscopic approach to cystectomy for invasive cancer in a 64-year-old female.<sup>27</sup> Operating room time was 8 hours, blood loss was minimal, and the postoperative course was free of complications. Puppo et al<sup>28</sup> performed laparoscopically assisted transvaginal radical cystectomy in 5 female patients with bladder cancer. Operating times were between 6 and 9 hours. Four of the 5 patients were discharged from hospital free of complications on days 7–11. The largest series of laparoscopic radical cystectomy was published by an Egyptian group. Denewer et al<sup>29</sup> reported on 10 patients with invasive bladder cancer, who underwent laparoscopically assisted cystectomy and urinary diversion. They demonstrated that the laparoscopic access involves less morbidity and earlier recovery as well as shorter hospital stay.

The Department of Urology at Charité Hospital in Berlin began its experience with laparoscopic radical cystectomy and urinary diversion in March 2000 to treat patients with muscle invasive bladder cancer.

### *Technique of laparoscopic radical cystectomy*

Preoperative preparation includes a bowel preparation with a clear liquid diet starting preoperative day 2; a 3 liters mechanical bowel on pre-operative day 1; and a cephalosporin and metronidazole on call to the operating room. The patient is placed supine with steep Trendelenburg position, and a six-port transperitoneal laparoscopic access is established (Figure 37.1). As in the open procedure, the right-handed surgeon stands to the patient's left. Camera monitors are positioned at the patient's feet. In our experience, dissection is best accomplished via laparoscopic scissors attached to



**Figure 37.1** Number and placement of trocars.

monopolar cautery in one hand of the surgeon, and graspers attached to bipolar cautery in the other. The first assistant utilizes suction in one hand and graspers for retraction in the other. We commonly utilize the Aesop robotic arm and voice recognition to give control of the camera to the surgeon. However, if the first assistant is being instructed, it is best to have a second assistant operate the camera.

Bilateral pelvic lymph node dissections are performed, removing tissue from the obturator fossa, and external iliac vein and artery from the obturator fossa up to the bifurcation of the aorta. The ureters are mobilized from the iliac vessel crossover to their entry into the bladder. Next, the peritoneum over the pouch of Douglas is incised and the vasa deferentia (in male) identified. Each vas is dissected towards the seminal vesicles, which are completely mobilized. The vasa deferentia and seminal vesicles are lifted anterior-superiorly, so that Denonvilliers' fascia can be incised, and the plane between the prostate and the rectum can be developed. In females, the pouch of Douglas is incised, and the posterior wall of the vagina is mobilized from the rectum. Also both ovaries are mobilized after transection of the ovarian vessels.

The dissection now turns anterior, where the peritoneum over the umbilical ligaments is incised, and the ligaments transected. The space of Retzius is developed as in the open procedure, with the urinary bladder dissected off the anterior abdominal wall, and the endopelvic fascia exposed. The endopelvic fascia is incised bilaterally, and the puboprostatic or pubourethral (women) ligaments divided. The dorsal vein complex is sutured with an 0-Vicryl purse-string, but not divided at this point.

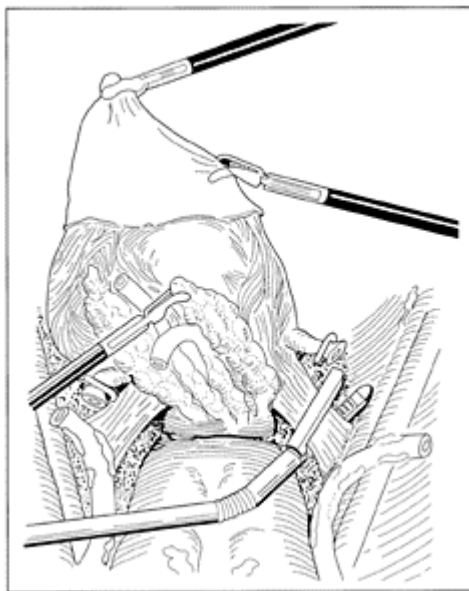
The posterior and anterior pedicles of the bladder and the pedicles of the prostate or uterus are divided by serial applications of the Endo-GIA stapler (Figure 37.2). The dorsal vein complex is now divided just proximal to the suture. The urethra is divided close to the pelvic floor, the catheter is removed, and the bladder neck is closed with a suture to avoid spillage of urine into the peritoneal cavity with the risk of tumor seeding. In men, the remaining attachments are divided to completely free the specimen (bladder, prostate, and seminal vesicles), which is secured in an endobag for later removal during



the urinary diversion. In women, the bladder with the anterior wall of the vagina are removed to complete the dissection, and the specimen is entrapped in an endobag for immediate removal through the vaginal opening. The vagina is then closed by a running 0-Vicryl suture.

### *Urinary diversion*

Once laparoscopic radical prostatectomy has been mastered, the only additional simple steps radical cystec



**Figure 37.2** Transection of the bladder pedicles with an Endo-GIA stapler.

tomy involves are taking down the lateral pedicles with the Endo-GIA stapler. The challenge is the urinary diversion.

The ileal loop urinary diversion has been the standard type of urinary diversion since it was described by Bricker in 1950.<sup>30</sup> The first laparoscopic ileal loop urinary conduit was reported by Kozminski and Partamian.<sup>31</sup> Their procedure did not include a cystectomy. A total of five port sites were used, one of which served as the stoma site. Laparoscopically, both ureters were mobilized and transected. The bowel anastomosis was performed extracorporeally by gently elevating a small loop of ileum through a port site. The initial operation took 6 hours and 20 min. De Badajoz et al<sup>27</sup> and Puppo et al<sup>28</sup> provided their patients with an ileal conduit after a laparoscopic cystectomy, as described before.

To date, most authors perform a laparotomy after laparoscopic cystectomy to remove the specimen and construct the urinary diversion (ileal conduit). However, Gill et al<sup>32</sup> have recently reported on an ileal conduit urinary diversion by laparoscopy alone,

performed in two men: the surgical times of the complete procedure (laparoscopic cystectomy and ileal conduit) were 11.5 and 10 hours and blood losses were 1200 and 1000 ml. However, most patients motivated and healthy enough to undergo a 10-hour laparoscopic procedure will also be the type of patients desiring the long-term quality of life aspects of a continent urinary diversion as well as the short-term recovery benefits of a laparoscopic approach. Most patients willing to accept the longer operative time required for a laparoscopic approach will also desire a continent urinary diversion because of the better quality of life and cosmesis.

The first experimental laparoscopic ureterosigmoidostomy for urinary diversion using pigs was reported by Trinchieri et al.<sup>33</sup> Anderson et al<sup>34</sup> published their experience constructing a laparoscopically assisted sigma rectum pouch as a continent urinary diversion in an animal model (pig). The laparoscopically mobilized sigma was extracorporeally positioned via a laparotomy. The pouch was formed by side-to-side anastomosis of the opened bowel segment with a stapler, and the ureterocolonic anastomoses were done extracorporeally. Postoperative function of the pouch was good. However, in 44% of the cases the formation of stones was diagnosed in the area of titan clips and in 33% stenosis of the ureterocolic anastomosis occurred. Denewer et al<sup>29</sup> used the same technique in 1999 for continent urinary diversion after laparoscopic cystectomy in his 10 patients. An 8 cm long incision in the lower abdomen was required to construct the sigma rectum pouch extracorporeally using a stapling technique, and the ureters were implanted in an antireflux fashion. No postoperative follow-up information was provided regarding stone formation.

The most noticeable benefit of the sigma rectum pouch diversion is the easy construction and the nearly 100% day- and night-time continence of properly selected patients. The sigma rectum pouch is a modification of the ureterosigmoidostomy and was first described by Fisch et al<sup>35</sup> as an alternative continent urinary diversion. Several authors reported excellent functional results of this continent urine reservoir after open radical cystectomy.<sup>36–38</sup>

To our knowledge, we performed the first continent urinary diversion completely laparoscopically in April 2000 at Charité Hospital, Berlin, using the Mainz pouch II technique.<sup>39</sup> Another issue of the laparoscopic procedure is how to remove the cystectomy specimen. Until now, laparoscopists have made a minilaparotomy for specimen removal. The opening of the sigmoid and rectum or the vagina also allows removal of the specimen without enlarging any of the abdominal port sites.

#### *Technique—laparoscopic Mainz II pouch (rectum sigma pouch)*

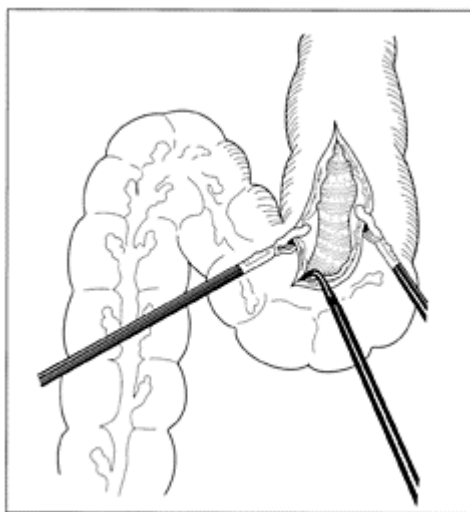
Prior to surgery, patients undergo outpatient sigmoidoscopy to exclude diverticulosis or other abnormalities. Further selection criteria include a competent anal sphincter, assessed by the ability to hold a 200–300 ml water enema for 2 hours, and adequate renal function (serum creatinine <1.5 mg/Dl).

An antimesenteric enterotomy is made with an electric hook at the recto-sigmoid junction and extended 10 cm proximally and 10 cm distally (Figure 37.3). In men, this allows for transanal removal of the specimen (Figure 37.4). The posterior walls of the rectum and sigmoid are then anastomosed side-to-side with a running 3–0 Maxon suture to form the posterior wall of the pouch (Figure 37.5). Nonrefluxing ureteral anastomoses

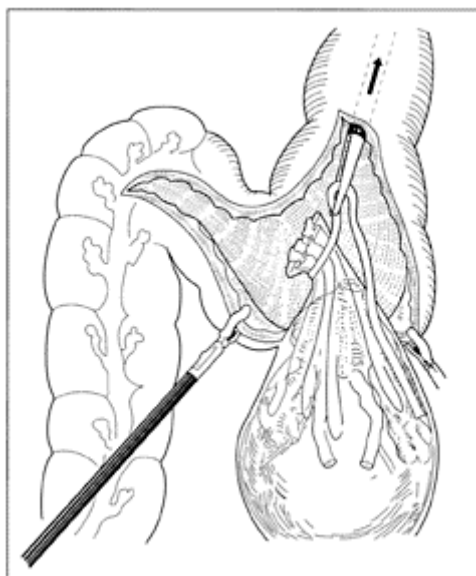
are formed by preparing a 3 cm submucosal bed in the posterior plate of the pouch, and then drawing the mobilized ureters through the pouch plate and securing them with 3–4 sutures in this previously formed bed. After insertion of 8F monopigtail ureteral catheters (via the opened rectum), the submucosal tunnels are completed by suturing the mucosa over the ureters (Figure 37.6). The ureteral stents are brought out of the anus and the pouch is drained with a transanal 26F Nélaton catheter. The anterior wall of the pouch is closed with a running 3–0 Maxon suture (Figure 37.7). The pelvis is drained with a single Jackson-Pratt (JP) drain through one of the lateral 5 mm trocar incisions. Hemostasis is checked, all trocars are removed under vision, and the trocar sites closed with running sutures.

### *Results*

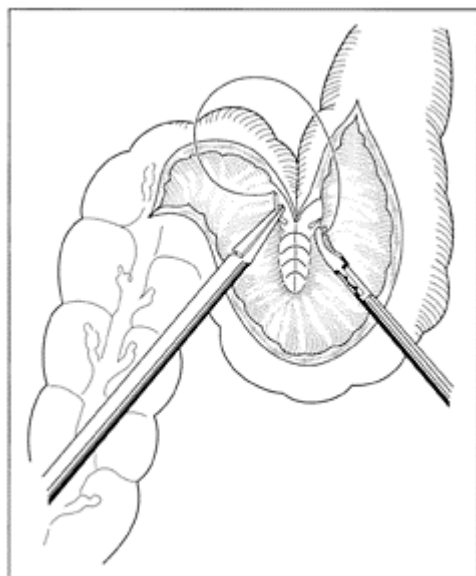
From April 2000 until October 2002, 13 patients (7 male, 6 female) diagnosed with clinical T2N0M0 transitional cell carcinoma of the bladder were selectively offered



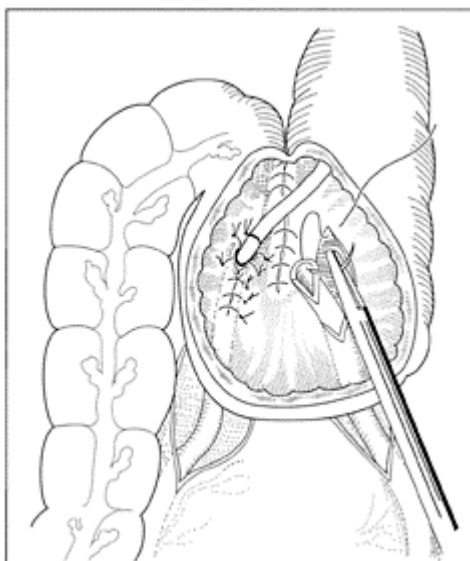
**Figure 37.3** Opening of the sigmoid intestine (antimesenterically) with electric hook.



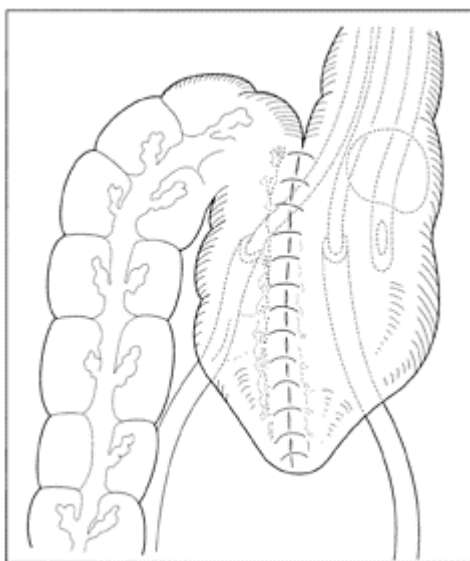
**Figure 37.4** Removal of the specimen in the endobag via the opened rectum.



**Figure 37.5** Side-to-side anastomosis of rectum and sigmoid to form the posterior wall of the pouch.



**Figure 37.6** Suturing of the mucosa of the sigmoid over the already implanted ureter to create the submucosal tunnel (nonrefluxing anastomosis).



**Figure 37.7** The anterior wall of the pouch is closed with running suture

(Maxon 3×0). Both ureters were stented with 8F ureteral catheters and the pouch was drained with a 26F Nélaton catheter.

laparoscopic radical cystectomy with continent urinary diversion—the Mainz II sigma rectum pouch. Prior to initiating this laparoscopic approach, 36 open cystectomies with Mainz II pouch diversions had been performed at Charité Hospital in Berlin. The mean age was 64.7 years old (range 58–69). The Mainz II diversion was selected for males with tumors infiltrating the prostatic urethra (orthotopic neobladder therefore contraindicated) or because they preferred this procedure to open surgery. In females the Mainz II pouch had already been our continent urinary diversion of choice before we started with the laparoscopic approach.

All 13 procedures were completed laparoscopically without intraoperative complications. Conversion to open surgery was required in no case. The median operating time was 6.3 hours (range 5.5–7.9). The median estimated blood loss was 220 ml (range 150–300 ml, 0 transfusions), and approximately 2500 ml of combined crystalloid/colloid intravenous fluids were required per the discretion of the anesthesiologist. In general, liquids were tolerated on postoperative day (POD) 2, the JP drain was removed POD 4, the ureteral stents were removed POD 8, and the pouch drain was removed POD 9. On POD 10, IVPs were performed, demonstrating normal upper tracts and no leakage from the pouch. Patients were discharged POD 10–12 (median 11), significantly earlier than patients after comparable open surgery in the German context. All patients are fully continent (day/night) of urine and stool. The only complication was a pouch leak at 3 weeks followup, repaired by open suturing. Histopathologic examination of the specimens revealed transitional cell carcinoma: pT1 G3+carcinoma-in-situ ( $n=1$ ); pT2b G2–3 ( $n=4$ ); pT3a G3 ( $n=5$ ); and pT3b G3 ( $n=3$ ). The resection margins were free of tumor in all specimens. Positive lymph nodes were detected in 1 patient, who was treated with adjuvant chemotherapy. Follow-up ranges are 1–27 months and has shown no local or systemic recurrence so far. In all patients, the upper urinary tract is still well preserved without any evidence of hydronephrosis. The renal function is normal and a mild hyperchloremic acidosis, compensated with oral sodium bicarbonate, occurred in 11/13 cases.

In our experience, the laparoscopic sigma rectum pouch has significant technical advantages as a ‘first-step’ continent urinary diversion. The sigmoid and rectum have posterior attachments that keep them fixed and facilitate laparoscopic suturing. Also, suture lines are significantly shorter than for an ileal neobladder. The rectum has a capacity of approximately 400 ml, and therefore only a 20 cm opening is needed along the sigmoid and rectal surface to form a detubularized, low-pressure pouch. Although endostapler devices could speed up the bowel closure, we only use absorbable sutures to minimize the chance of future stone formation.

It is important to emphasize that the sigma rectum pouch is not a traditional ureterosigmoidostomy, nor should it be associated with the significant complications and secondary cancers in connection with that abandoned procedure. Gumus et al have demonstrated, by filling cystometry, that the sigma rectum pouch holds 400 ml of urine without reflux into the descending colon or ureters.<sup>40</sup> In reports of the classic

ureterosigmoidoscopy, urine and stool were stored together in the rectum, and it was thought that urine frequently refluxed up the colon caused by frequent contractions that led to frequent fecaluria. Chronic irritation of the ureteral anastomoses with fecal material was thought to predispose future cancer growths.<sup>41</sup>

The sigma rectum pouch provides the fixation of the left descending colon to the rectal ampulla in order to keep the colon in line with the rectum. The result is that the majority of our patients reported separately passing urine and feces at convenient intervals and with good anal control. Since urine and stool are not constantly mixed because ureteral anastomoses are away from the path of stool, it has been proposed that the risk of carcinogenesis should be significantly lower.<sup>42</sup> Nevertheless, long-term follow-up to determine the incidence of colonic carcinogenesis and ureteral strictures is limited.

Despite the advantages of continence and ease of construction with the sigma rectum pouch, the ileal neobladder remains the favored continent urinary diversion. In cases where it is not appropriate or desired to divert to the urethra, the sigma rectum pouch is a viable alternative and feasible to construct laparoscopically. Further functional follow-up and quality of life studies will be needed to determine its equivalence or superiority. In the meantime, Kaouk et al<sup>43</sup> have recently reported success with laparoscopic construction of an ileal neobladder in a pig model, and we anticipate working towards this clinical goal in the near future. Regardless of the form of laparoscopic diversion, the relatively low intravenous fluid requirements during these procedures (2500 ml combined crystalloid/colloid) suggests the intriguing possibility of less fluid shifts and electrolyte loss, and overall cardiovascular stress to the patient is reduced, which is another potential benefit that needs further study.

## Summary

The last decade has seen promising advances in laparoscopic urologic surgery. What once was thought technically impossible is now becoming a reality. While early laparoscopy was mostly used for ablation of diseased tissue, it has changed and has now become a tool for reconstruction as well. While reconstructive laparoscopy still remains challenging, advances in clip and suture technology have been of great benefit. These advances have enabled radical cystectomy and construction of a continent urinary diversion to be performed by the laparoscopic approach alone, while established oncologic and reconstructive principles are maintained. But laparoscopic cystectomy and urinary diversion are still in their infancy. A number of problems will need to be addressed before such complicated procedures become commonplace. The future will surely see further improvements in instruments for reconstruction plus the application of novel energy sources to achieve more rapid, yet accurate approximation of tissue.

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## Urothelial tumors of the renal pelvis and ureter

Peter A Pinto and Thomas W Jarrett

### **Incidence/epidemiology/ etiology**

Transitional cell carcinoma (TCC) involving the renal pelvis accounts for approximately 10% of all renal tumors and 5% of all urothelial tumors.<sup>1</sup> Tumors involving the ureter are even less common. Upper tract urothelial tumors most commonly affect patients in their sixth to seventh decade of life.<sup>2</sup> Occurrence of these tumours is approximately twice as common in males as in females<sup>3</sup> and they are more commonly seen in whites.<sup>4</sup>

The preceding statistical information is different for cases involving Balkan nephropathy: this is degenerative interstitial nephropathy, which is endemic to rural areas of Balkan countries, and is believed to be related to increased exposure to radon and minerals in the water.<sup>5</sup> These cases have a much higher incidence of upper tract urothelial cancers.

Approximately 2–4% of bladder cancer cases develop upper tract disease, although this could be as high as 25% in cases of bladder carcinoma-in-situ.<sup>6</sup> Patients with initial upper tract TCC develop bladder cancer in 25–75% of cases.<sup>7</sup>

Multiple factors can contribute to the development of upper tract TCC, and they are most likely similar to the causes of urothelial carcinoma involving the bladder. The most important causes are cigarette smoking, exposure to occupational carcinogens, analgesics, coffee, cyclophosphamide, and chronic infections and stones.

### **Presentation**

Gross hematuria is the most common presenting symptom, accounting for approximately 75% of cases.<sup>8</sup> Those patients who develop renal colic can experience dull pain as the tumor grows and obstructs, or acute pain from clot colic. Other presenting symptoms are similar to those found with lower tract urothelial carcinoma.

### **Diagnosis**

Imaging studies such as intravenous pyelography (IVP), computed tomography (CT), ultrasonography, and magnetic resonance imaging (MRI) are usually the first diagnostic procedures undertaken when one suspects upper tract urothelial carcinoma.

IVP has been the most commonly performed study revealing a radiolucent filling defect in approximately 50–75% of cases.<sup>8</sup> High-grade ureteral tumors can cause nonvisualization of the renal unit or severe hydronephrosis.

Recently, there has been debate over the ideal imaging study for hematuria. Contrast CT scans are arguably as good or better for detecting urologic pathology.<sup>9</sup> This imaging modality also provides staging information along with unveiling pathology outside the urinary tract.

Not all filling defects can be attributed to malignant processes. Benign conditions such as calculi, blood clots, sloughed papillae, fungal balls, endometriosis, tuberculosis, ureteritis or pyelitis cystica, and vascular phenomena can present in a similar fashion.<sup>10</sup> In addition, before determining if a patient is a candidate for endourologic management, one needs to know the grade and location of the urothelial carcinoma. Therefore, before planning definitive treatment, retrograde pyelography and ureteropyeloscopy may be necessary. Selective urine cytology, brush cytology, or biopsy of the lesion can be obtained at the same setting to confirm the diagnosis and determine the grade of the lesion.

### **Pathology**

More than 90% of upper tract urothelial tumors are TCC.<sup>11</sup> Less than 10% are attributed to squamous cell carcinoma and less than 1% to adenocarcinoma. These are both usually associated with stones and inflammation.<sup>12,13</sup> Although rare, inverted papillomas, sarcomas, fibroepithelial polyps, and metastatic lesions can involve the upper tract.

### **Endoscopic treatment and results**

The propensity of upper tract TCC towards ipsilateral recurrence and the limitations of upper tract endoscopy have led to radical nephroureterectomy as the gold standard treatment.<sup>14</sup> Even though the cancer-related risks are greater for any alternative treatment, in some select patients the risk of major open surgery or chronic renal failure outweighs the risks of cancer.<sup>15</sup> In other patients with small volume of low-grade disease, the risk of progression is minimal.<sup>16</sup> Thus, the removal of the entire renal unit may not be warranted in a situation where the tumor can be safely removed endoscopically. Recent advances in technology and techniques have permitted the effective endourologic management of upper tract TCC, thus allowing renal-sparing therapy. Still the gold standard is radical nephroureterectomy. Although traditionally performed open, advances in laparoscopic techniques have allowed minimally invasive surgery to play a role. The history, techniques, and results of endoscopic management of upper tract TCC will now be discussed.

In 1912, Hugh Hampton Young described the first endoscopic evaluation of the upper urinary tract.<sup>17</sup> Subsequent advances in techniques and technology allow us to reach all parts of the urinary tract with minimal morbidity via antegrade and retrograde approaches. Diagnosis and treatment of upper tract TCC have become possible with these improvements, as tumor biopsy and ablation using various energy sources is possible even through the smallest of instruments. In addition, miniaturization has made follow-up surveillance of the upper tract more practical with the use of smaller ureteroscopes, which usually do not require previous stenting, or active dilation of the distal ureter.

Tumors of the upper urinary tract can be approached in a retrograde or antegrade fashion. The approach chosen depends largely on the tumor location and volume. In general, a retrograde ureteroscopic approach is used for low-volume ureteral and renal tumors. An antegrade percutaneous approach is preferred for larger tumors of the upper ureter or kidney, or those which cannot be adequately manipulated in a retrograde approach due to location (i.e. lower pole calyx) or previous urinary diversion. In cases with multifocal involvement, a combined antegrade/retrograde approach can be considered.

The basic principles for treating TCC of the upper urinary tract are similar to those of the bladder counterpart. The tumor is biopsied and ablated using electrocautery or laser energy sources. A staged procedure should be considered for high-volume disease or disease that is thought to represent high pathologic grade and/or stage. In such cases where subsequent nephroureterectomy will be most likely to be necessary for cure, biopsy and partial ablation is done to minimize the risks of perforation or major complications. Endoscopic management is completed only after the pathology shows the patient is an acceptable candidate for continued minimally invasive endoscopic management. If the pathology is unresectable, high grade, or invasive, the patient should proceed immediately to nephroureterectomy provided he is medically fit. In addition, patients accepting renal sparing therapy must be committed to a lifetime of follow-up with radiographs and endoscopy.

### *Retrograde approach*

The ureteroscopic approach to tumors was first described by Goodman in 1981 and is generally favored for ureteral and smaller renal tumors. With the advent of small-diameter rigid and flexible ureteroscopes, tumor location is not as much of a limiting factor as previously thought. The advantages of a ureteroscopic approach are mainly low morbidity when compared to the percutaneous and open surgical counterparts and the maintenance of a closed system. With a closed system, nonurothelial surfaces are not exposed to the possibility of tumor seeding.

The major disadvantages of a retrograde approach are related to the smaller instruments required. The smaller endoscopes have a smaller field of view and working channel. This limits the size of tumor that can be approached in a retrograde fashion. In addition, all portions of the upper urinary tract, such as the lower pole calyces, cannot be reliably reached with working instruments. The smaller instruments limit the ability to remove large volumes of tumor and obtain deep specimens for reliable tumor staging. Retrograde ureteroscopy is difficult in patients with prior urinary diversion.

### **Technique and instrumentation**

A wide variety of ureteroscopic instruments are available, each with its own distinct advantages and disadvantages. In general, rigid ureteroscopes are used primarily for the distal and midureter. Access to the upper ureter and kidney with rigid endoscopy is unreliable, especially in the male patient. Larger, rigid ureteroscopes provide better visualization because of their larger field of view and better irrigation. Smaller rigid

ureteroscopes (8F) are generally preferred, as they do not require active dilation of the ureteral orifice.

Newer-generation flexible ureteropyeloscopes are now available in sizes less than 8F, which facilitates simple and reliable passage to all portions of the urinary tract.<sup>18,19</sup> These are generally preferred in the upper ureter and kidney, where the rigid ureteroscope cannot be reliably passed. Flexible ureteroscopes, however, have technical limitations such as a small working channel, which limits irrigant flow and the diameter of working instruments. Further limitations of flexible ureteroscopy include access to certain areas of the kidney, such as the lower pole, where the infundibulopelvic angle may limit passage of the scope or prior urinary diversion.

**Endoscopic evaluation and collection of urinary cytology.** Cystoscopy is performed and the bladder inspected for concomitant bladder pathology. The ureteral orifice is identified and inspected for lateralizing hematuria. A retrograde pyelogram is performed to show upper tract anatomy and possible filling defects. A small-diameter ureteroscope is passed directly (6.9 or 7.5F) into the ureteral orifice and the distal ureter inspected prior to any trauma from a previously placed guide wire or dilation. A guide wire is then placed through the ureteroscope and up the ureter to the level of the renal pelvis under fluoroscopic guidance. The flexible ureteroscope is used to visualize the remaining urothelium. When a lesion or suspicious area is seen, a normal saline washing of the area is performed before biopsy or intervention.<sup>20</sup> If the ureter will not accept the smaller ureteroscope, acute dilation of the ureter will be necessary.

Special circumstances include patients with prior urinary diversion and tumor confined to the intramural ureter. With cases of prior urinary diversion, identification of the ureteroenteric anastomosis is difficult and may require antegrade percutaneous passage of a guide wire down the ureter prior to endoscopy. The wire can be retrieved from the diversion and the ureteroscope can be passed in a retrograde fashion. The nephrostomy tract need not be fully dilated in this setting. A second situation is a tumor confined to the intramural tumor. In such cases where tumor is seen protruding from the ureteral orifice, aggressive transurethral resection of the entire most distal ureter can be done with acceptable results.<sup>21</sup>

**Biopsy and definitive treatment.** The following three general approaches can be used for tumor ablation:

- bulk excision with ablation of the base
- resection of the tumor to its base
- diagnostic biopsy followed by ablation with electrocautery or laser energy sources.

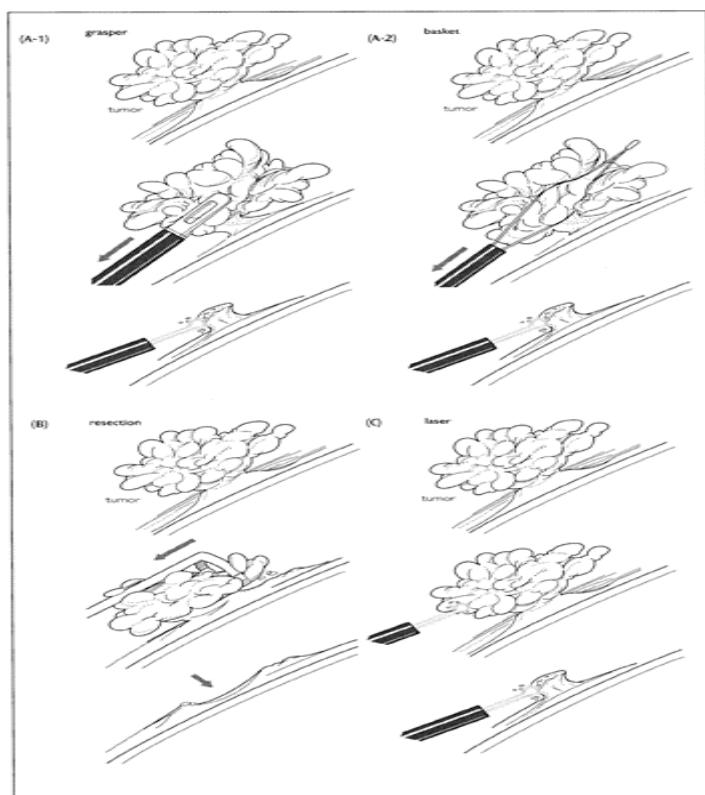
Regardless of the technique used, special attention to biopsy specimens will be necessary. Specimens are frequently minute in size, should be placed at once in fixative, and specifically labeled for either histologic or cytologic evaluation.<sup>22</sup> The pathologist is asked to review the specimen to evaluate the adequacy of the tissue submitted and to coordinate the method of its pathologic processing.

**Ureteroscopic techniques.** The tumor is debulked using either grasping forceps (Figure 38.1A-1) or a flat wire basket (Figure 38.1A-2) engaged adjacent to the tumor. The tumor base is then treated with either electrocautery or laser energy sources. This technique is especially useful for low-grade papillary tumors with a narrow stalk. The specimen is sent for pathologic evaluation.

A ureteroscopic resectoscope is used to electrosurgically remove the tumor (Figure 38.1B). Only the intraluminal tumor is resected and no attempt is made to resect deep (beyond lamina propria) as one would with a bladder tumor due to the high risk of perforation. Extra care is necessary in the mid and upper ureter where the wall is quite thin and prone to perforation. Ureteral resectoscopes tend to be larger (12F) and require active dilation of the ureteral orifice. With larger-volume disease of the distal ureter, Jarrett and associates described extensive dilation of the ureter followed by resection with a long standard resectoscope.<sup>23</sup>

The tumor is adequately biopsied and sent to pathology for diagnostic evaluation. The tumor bulk is then ablated to its base using laser or electrosurgical energy (Figure 38.1C). Multiple biopsy specimens are usually required, especially when using the small flexible 3F biopsy forceps. Electrosurgery delivered via a small Bugbee electrode (2 or 3F) can be used to fulgurate tumors. The variable depth of penetration can make use in the ureter quite dangerous. Thus, fulguration circumferentially or of a large area should be avoided due to the high risk of stricture formation. More recently, laser energy with either neodymium:YAG<sup>24–26</sup> or holmium:YAG<sup>27,28</sup> sources has been popular. Each has characteristic advantages and can be delivered through a small flexible fiber (200 or 365  $\mu\text{m}$ ), allowing for delivery of energy even through small flexible ureteroscopes without significantly altering irrigant flow or scope deflection.

The holmium:YAG laser is well suited for use especially in the ureter. With a tissue penetration less than 0.5 mm, it can safely ablate tumor with excellent hemostasis and minimal risk of full-thickness injury to the urothelium. However, its shallow depth of penetration may make its use cumbersome with larger tumors, especially in the renal pelvis. Settings most commonly used are an energy of 0.6–1.0 J with a frequency of 10 Hz. The neodymium:YAG laser has a tissue penetration of up to 5–6 mm, depending on laser settings and duration of treatment. Unlike the holmium laser, which ablates tumor, the neodymium:YAG laser works by coagulative necrosis, with subsequent sloughing of the necrotic tumor. The safety margin is significantly lower and can limit its safe use in the ureter where the ureteral wall is quite thin. Settings most commonly used for the neodymium:YAG laser are 15 W for 2 s duration for ablating tumor and 5–10 W for 2 s for coagulation. A ureteral stent is placed for a variable duration to aid with the healing process. Large tumors usually require multiple treatment sessions over several months.



**Figure 38.1** Techniques for ureteroscopic treatment of ureteral and renal tumors. (A-1) The tumor is identified and removed piecemeal using grasping forceps to its base. (A-2) Alternatively, a flat wire basket can be deployed alongside the tumor. The tumor is engaged and removed with care not to avulse the adjacent ureter. With either of these techniques, the base is treated with electrocautery or a laser energy source. (B) The tumor is identified and removed using a ureteroscopic resectoscope. The technique differs from the technique for bladder tumors in that only

intraluminal tumor is resected. No attempt is made to resect deep, as with a bladder tumor. The scope is not arching deep into the tissue. (C) The tumor is biopsied for diagnostic purposes. The bulk of the tumor is then ablated using electrosurgical or laser energy. Laser energy is generally preferred because it has more reliable delivery of energy and depth of penetration. The two most commonly used energy sources are holmium:YAG and neodymium:YAG (Reproduced with permission of Elsevier Science from Sagalowsky AI, Jarrett TW. Management of urothelial tumors of the renal pelvis and ureter. In: Walsh PC, Retik AB, Vaughan ED Jr, Wein AJ, eds. *Campbells urology*, 8th edn, Vol.4. Philadelphia: WB Saunders, 2002:2845–75.)

### **Results of retrograde approach**

Multiple series have shown the safety and efficacy of ureteroscopic treatment of upper tract TCC.<sup>29–31</sup> In a literature review of 205 patients, the overall recurrence rate for ureteral and renal pelvic lesions was 33% and 31.2%, respectively, and the risk of bladder recurrence was 43%.<sup>32</sup> In the two largest series there was a single cancer death directly attributed to recurrent upper tract disease.<sup>31</sup> As with any TCC, the most important prognostic indicator for tumor recurrence was grade. Keeley and associates showed a recurrence rate of 26% for grade 1 tumors and 44% for grade 2, which roughly correlates with previously established recurrence rates for open conservative surgery.<sup>33</sup>

Procedure complications were uncommon and usually related to patient comorbidities. Complications specific to ureteroscopic therapy included ureteral perforation, which can be managed with indwelling ureteral stent and ureteral stricture. Stricture formation ranged from 5 to 13%.<sup>29–31</sup> The complication rates have dropped in more contemporary series, most probably related to smaller endoscopes, improved laser energy sources, and refinements in endoscopic techniques.

Two major concerns of the ureteroscopic approach are the accuracy of ureteroscopic biopsies and the limitations of biopsies, especially with regard to staging.<sup>34</sup> Retrospective reviews of patients who underwent ureteroscopic biopsy followed by nephroureterectomy found the accuracy of ureteroscopic diagnosis to be 89–94% and the pathologic grading



to match the open surgical technique in 78%-92%.<sup>31,35</sup> From prior studies we know that there is an excellent correlation between grade of the lesion and stage.<sup>36,37</sup> This holds true for the ureteroscopic approach, because 87% of patients with grade 1 or 2 tumors had noninvasive disease (Ta or T1), whereas 67% of patients with grade 3 tumors had invasive disease (T2 or T3).<sup>33</sup> This information supports the notion that tumor grade is the most important prognostic factor and, although stage cannot be directly assessed, noninvasive disease can be expected in most cases of low-grade tumor.

A final concern is whether the ureteroscopic approach promoted progression of local disease to other urothelial surfaces or metastatic disease. There have been reports of increased tumor appearance in refluxing ureters of patients with bladder tumors<sup>38</sup> and in the ipsilateral urinary tract and bladder following ureteroscopic treatment. However Kulp and Bagley reported on 13 patients who underwent multiple ureteroscopic treatments followed by nephroureterectomy and found no unusual propagation of TCC in the specimens.<sup>39</sup> Concerns that ureteroscopy may promote metastatic spread were raised by Lim and associates, who found tumor cells in renal lymphatics after ureteroscopy.<sup>40</sup> However, Hendin and associates showed no increased risk of metastatic disease in a group of patients who underwent ureteroscopy prior to nephroureterectomy when compared to those undergoing nephroureterectomy alone.<sup>41</sup>

### *Antegrade approach*

The percutaneous approach was first described by Tomera et al in 1982 and is generally favored for larger tumors located proximally in the renal collecting system and/or proximal ureter.<sup>42</sup>

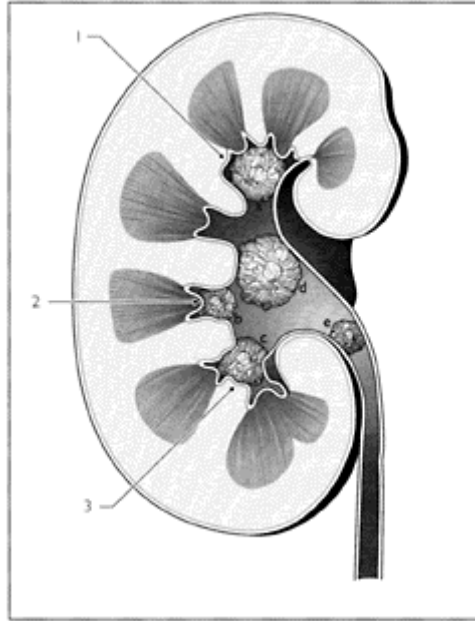
The main advantage of the percutaneous approach is the ability to use larger instruments, which can remove a large volume of tumor in any portion of the renal collecting system. Since deeper biopsies are obtained, tumor staging as well as grading is possible. In addition, a percutaneous approach may avoid the limitations of flexible ureteroscopy, especially when working in a complicated calyceal system or difficult areas to access such as the lower pole calyx or the upper urinary tract of patients with urinary diversion. With a percutaneous approach, the established nephrostomy tract can be maintained for immediate postoperative nephroscopy and administration of topical adjuvant therapy.

The main disadvantages are the increased morbidity compared with ureteroscopy and the potential for tumor seeding outside the urinary tract. Establishment of the nephrostomy tract has inherent risks and usually cannot be done as an ambulatory procedure. Distinct risks related to percutaneous removal are loss of urothelial integrity and exposure of nonurothelial surfaces to tumor cells. This open system provides the possibility of tumor implantation in the nephrostomy tract.

### **Technique and instrumentation**

**Establishment of the nephrostomy tract.** Under a single general anesthesia, cystoscopy is performed and an opened ureteral catheter is positioned in the pelvis. Contrast is injected through the ureteral catheter to define the calyceal anatomy, and a percutaneous nephrostomy tract is established through the desired calyx (Figure 38.2). Tumors in

peripheral calyces are best approached with direct puncture distal to the tumor. Disease in the renal pelvis and upper ureter is best approached through an upper or middle pole access so as to allow scope maneuvering through the collecting system and down the ureteropelvic junction. The tract is dilated using either sequential (Amplatz) or balloon dilation so as to accommodate a large 30F sheath. Correct positioning of the nephrostomy tract is crucial to the success of the procedure and should be performed by the urologist or by the radiologist after direct consultation with the operating surgeon.



**Figure 38.2** Nephrostomy tract puncture site. The position of the nephrostomy is imperative for successful percutaneous resection of transitional cell carcinoma of the renal collecting system and upper ureter and requires careful preoperative evaluation of radiographs for tumor location. Tumors located in peripheral calyces (A-C) are best approached by direct puncture as far distally in the calyx as possible. Tumors located in the renal pelvis (D) and upper ureter (E) are best approached by puncture to

an upper (1) or middle (2) calyx, which allows the scope to be maneuvered in the renal pelvis and down the ureter.

Lower calyx puncture (3) for tumor in the lower calyx. (Reproduced with permission of Elsevier Science from Sagalowsky AI, Jarrett TW.

Management of urothelial tumors of the renal pelvis and ureter. In: Walsh PC, Retik AB, Vaughan ED Jr, Wein AJ, eds. *Campbells urology*, 8th edn, Vol. 4. Philadelphia: WB Saunders, 2002:2845–75.)

A nephroscope is inserted and the previously placed ureteral catheter is grasped, brought out of the tract, and exchanged for a stiff guide wire, thus providing both antegrade and retrograde control and ensuring that access is not compromised with nephroscopy. Complete nephroscopy is performed using rigid and flexible endoscopes when necessary. Any suspicion of upper ureteral involvement warrants flexible antegrade ureteroscopy.

**Biopsy and definitive therapy.** Following identification, the tumors need to be removed using one of three following techniques (Figure 38.3). In the first technique, which uses a cold-cup biopsy forceps through a standard nephroscope, the bulk of the tumor is grasped using forceps and removed in piecemeal fashion until the base is reached (Figure 38.3A). A separate biopsy of the base is performed for staging purposes and the base is cauterized using a Bugbee electrode and cautery. Low-grade papillary lesions on a thin stalk are easily treated in this manner with minimal bleeding.

Alternatively, a cutting loop from a standard resectoscope is used to remove the tumor to its base (Figure 38.3B). Once again the base should be resected and sent separately for staging purposes. This approach is more effective for larger broad-based tumors where simple debulking to a stalk is not possible.

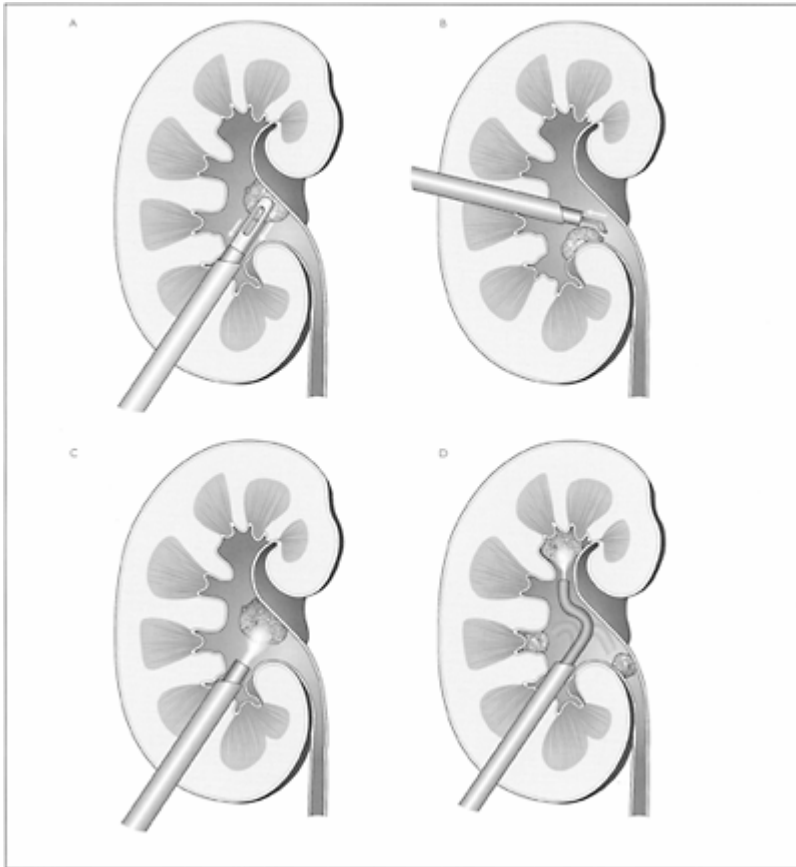
For the third technique, which uses flexible or rigid endoscopes, the tumor is biopsied and treated with holmium:YAG or neodymium:YAG laser at 25–30 W (Figure 38.3B, C, and D).

Regardless of technique, a nephrostomy tube is left in place. This access can be used for second-look followup nephroscopy to ensure complete tumor removal. Nephroureterectomy is indicated if the pathology shows high-grade or invasive disease.

**Second-look nephroscopy.** Follow-up nephroscopy is performed 4–14 days later to allow for adequate healing. At second-look nephroscopy, the tumor resection site is identified and any residual tumor is removed. If no tumor is identified, then the base should be biopsied, and treated using cautery or the neodymium:YAG laser (15–20 W and 3 s exposures). The nephrostomy tube can be removed several days later if all tumors have been removed. If the patient is being considered for adjuvant topical therapy, then a small 8F nephrostomy tube is left to provide access for instillations. Some authors have advocated a third-look nephroscopy prior to final nephrostomy tube removal.<sup>43</sup>

### Results of antegrade approach

Owing to the rarity of the disease, there are only several retrospective series with adequate numbers and follow-up to draw reasonable conclusions.<sup>43-45</sup> In a literature review of 84 patients, Okada and associates found an overall recurrence rate of 27%.<sup>46</sup> Tumor grade strongly predicted outcomes, as Jarrett et al<sup>43</sup> showed the recurrence rate for grades 1, 2, and 3 lesions to be 18, 33, and 50%, respectively. The only cancer-related mortalities in this series were in patients with high-grade disease. Lee et al reviewed their 13-year experience with percutaneous management, comparing 50 patients who underwent percutaneous management to 60 who underwent nephroureterectomy



**Figure 38.3** Techniques for percutaneous removal of transitional cell carcinoma of the renal collecting system. (A) The tumor is identified and debulked using forceps to its base.

The base is biopsied and sent separately for evaluation. This technique works well for papillary tumors on a narrow stalk. Broad-based tumors may cause excessive bleeding and are best approached with resection or laser therapy. (B) Using a standard resectoscope, the tumor is identified and resected to its base. Special care should be taken to avoid resection into major renal vasculature. The tumor is identified, biopsied for diagnostic purposes, and treated using holmium or neodymium laser sources. This can be done via a standard nephroscope (C) or using a flexible cystoscope (D). (Reproduced with permission of Elsevier Science from Sagalowsky AI, Jarrett TW. Management of urothelial tumors of the renal pelvis and ureter. In: Walsh PC, Retik AB, Vaughan ED Jr, Wein AJ, eds. *Campbell's urology*, 8th edn, Vol. 4. Philadelphia: WB Saunders, 2002:2845–75.)

and found no significant difference in overall survival.<sup>47</sup> As expected, patients with low-grade disease did well, regardless of modality chosen, and patients with high-grade disease did poorly, regardless of treatment option.

Most would agree from the literature that percutaneous management is acceptable in patients with low-grade (grade 1) disease, regardless of the status of the contralateral kidney, provided the patient is committed to lifelong follow-up. Patients with grade 3 disease do poorly, regardless of modality chosen, but should probably have the gold standard nephroureterectomy to maximize cancer therapy (provided they are medically fit). The largest area of controversy surrounds the use of percutaneous management for patients with grade 2 disease and a normal contralateral kidney. Jabbour et al retrospectively evaluated 24 patients and found a disease-specific survival of 95% overall, and 100 and 80% for stage Ta and T1 lesions, respectively.<sup>48</sup> This study shows an acceptable result with noninvasive grade 2 disease. With more invasive lesions, the potential for disease progression and metastatic disease are not insignificant and nephroureterectomy should be strongly considered.

Complications from percutaneous management of tumors are similar to those for benign renal processes and include bleeding, perforation of the collecting system, or

secondary ureteropelvic junction obstruction. Complications increased in number and severity with higher tumor grade.<sup>43</sup> This finding is probably due to the more extensive pathology and treatments necessary to eradicate the tumor. Unlike ureteroscopic resection, the percutaneous method was able to adequately stage tumors and, as expected, stage increased with tumor grade.

A major concern of the percutaneous approach is the potential seeding of nonurothelial surface with tumor cells. Although there have been several reported cases of nephrostomy tract infiltration with high-grade tumors,<sup>42,49,50</sup> there were no occurrences in the three largest series.<sup>43-45</sup> Tract seeding is a possibility but appears to be an uncommon event.

### **Adjuvant therapy**

Any procedure short of nephroureterectomy will have a higher local recurrence due to the established risk of ipsilateral recurrence. Several approaches are available to minimize these risks. These fall into two basic categories: instillation of immunotherapeutic or chemotherapeutic agents and brachytherapy of the nephrostomy tract.

#### *Instillation therapy*

Instillation therapy can be performed in several acceptable fashions. Accepted techniques include antegrade instillation via a nephrostomy tube (Figure 38.4), or retrograde via direct instillation into a ureteral catheter or by reflux in a patient with an indwelling ureteral stent or iatrogenically created vesicoureteral reflux. Patel and Fuchs described a convenient technique of outpatient instillation via a ureteral catheter placed suprapubically. Regardless of the technique chosen, administration to the upper urinary tract should be performed under low pressure and in the absence of active infection to minimize the risk of bacterial sepsis and/or systemic absorption of the agent.

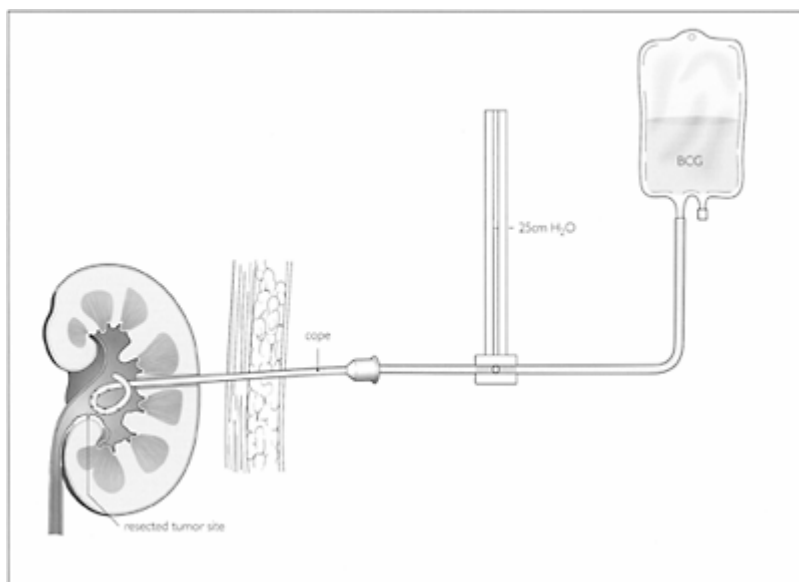
### **Results**

It makes clinical sense that the same agents used to treat urothelial carcinoma of the bladder would be effective in the upper urinary tract. Many studies have described small retrospective series of patients undergoing therapy with thiotepa,<sup>29,44</sup> mitomycin,<sup>30,31,51,52</sup> and bacille CalmetteGuérin BCG.<sup>43,51,53-55</sup> Although the cumulative experience appears convincing, no individual study has shown statistical improvement with relation to survival and recurrence rates. Possible reasons for this include:

1. insufficient numbers to show clinical significance owing to the relative rarity of the disease
2. tumors of the upper urinary tract have a different tumor biology than their bladder counterparts or
3. the delivery system is inadequate and, unlike the bladder, does not allow for uniform delivery of the agent with adequate dwell time to enable a clinical response.

No doubt further studies are required to settle this issue.

The most common complication of treatment is bacterial sepsis. In order to minimize this risk, patients must be evaluated for active infection prior to treatment and a low-pressure delivery system should be used. Agent-specific complications of the various therapies include ramification of systemic absorption of the agent. Specific to the upper urinary tract, Bellman et al described the complications of BCG following percutaneous management.<sup>56</sup> Most commonly seen was granulomatous involvement of the kidney in the absence of systemic signs of BCG infection. Mukamel et al saw an inordinate decrease in renal function among patients receiving BCG who had vesicoureteral reflux.<sup>57</sup>



**Figure 38.4** Set-up for administration of topical immunotherapy or chemotherapy to the upper urinary tract via a previously placed nephrostomy tube. Therapy is instilled via gravity with a mechanism that prevents excessive intrarenal pressures. High pressures have been linked to complications of systemic absorption and bacterial sepsis. (Reproduced with permission of Elsevier Science from Sagalowsky AI, Jarrett TW. Management of urothelial tumors of the renal pelvis and ureter. In: Walsh PC, Retik AB, Vaughan ED Jr, Wein

AJ, eds. Campbells urology, 8th edn,  
Vol. 4. Philadelphia: WB Saunders,  
2002:2845–75.)

### *Brachytherapy*

Brachytherapy to the nephrostomy tract via iridium wire or delivery system has been described by Patel et al<sup>44</sup> and Nurse et al.<sup>58</sup> There were no instances of tract recurrences in this series, although the authors acknowledge the rarity of the event. The only major complication that has been attributed to brachytherapy is fistula formation requiring nephroureterectomy.

### *Oral immunotherapy*

Propirimine is an oral agent which induces an interferon response in the urinary tract and thus is an immunotherapeutic agent. Early studies have shown some promise in the bladder and upper urinary tract but significant drop out due to drug-related toxicity.<sup>59</sup>

### **Follow-up**

The propensity of upper tract tumors towards multifocal recurrence and metastatic spread with more dysplastic lesions makes follow-up complicated. Postoperative evaluation must routinely include evaluation of the bladder, ipsilateral (if organ-sparing therapy was chosen), and contralateral urinary tracts, and of extraurinary sites for local and metastatic spread. A follow-up regimen is thus dependent on the time from surgery, the approach chosen (organ-sparing vs radical), and the potential for metastatic spread.

All patients should be assessed at regular 3-month intervals, the first year after being rendered tumor free, by endoscopic or open surgical approaches.<sup>31</sup> This is largely based on work with bladder TCC which shows that most tumor recurrences following bladder resection are in the first year.<sup>60,61</sup> The upper urinary tract is more difficult to monitor, and delayed recognition of upper tract tumor recurrence may lead to rapid disease progression and poor results.<sup>62</sup> Evaluation should include history, physical examination, urinalysis, urine cytology (for high-grade lesions), and office cystoscopy due to the high risk of bladder recurrences in patients treated both conservatively and with nephroureterectomy.<sup>62,63</sup> This is performed every 3 months for the first year, every 6 months for the next 2 years, and yearly thereafter. If the patient's primary pathology was high grade, a urine cytology may be helpful in assessing for tumor recurrence.<sup>63</sup> Its utility, however, is decreased with less dysplastic tumors.<sup>64–66</sup>

Bilateral disease, either synchronous or metachronous, is seen in 1–4% of patients,<sup>63,67,68</sup> and thus imaging of the contralateral kidney by intravenous urogram or retrograde pyelogram is required on a yearly basis. Retrograde pyelography may be necessary if the patient is not a candidate for contrast injection or if the intravenous urogram is not of adequate quality. In addition, CT or sonography may be helpful in distinguishing stones from soft tissue densities. Further evaluation of filling defects on imaging studies usually requires ureteroscopic evaluation. If the patient requires



endoscopic evaluation of the upper urinary tract, cystoscopy can be performed in conjunction with that procedure.

If an organ-sparing approach is chosen, the ipsilateral urinary tract must be assessed as well as the remainder of the urinary tract. The frequency and duration of the follow-up depends largely on the grade and stage of the lesion but is usually every 6 months for the first several years and yearly thereafter. Radiographic evaluation of the upper tracts alone is not adequate, as Keeley and associates showed that 75% of early tumor recurrences were visible endoscopically and not radiographically.<sup>31</sup> With tumors approached in a percutaneous fashion, immediate followup nephroscopy can be performed through the established nephrostomy tract.

The burden of repeated endoscopic evaluation of the upper urinary tracts used to be a major deterrent to conservative therapy in the past. The use of smaller 7.5F flexible ureteroscopes has greatly eased the burden of follow-up, as ureteroscopes can be reliably passed up the ureter without the need for dilation of the ureteral orifice or prior stenting. Others have advocated resection of the ureteral orifice to facilitate subsequent surveillance ureteroscopy in the office setting.<sup>69</sup> Even though technology has somewhat facilitated follow-up, both physician and patient must be committed to organ-sparing treatment.

Metastatic restaging is required in all patients at significant risk for disease progression to local or distant sites. This group encompasses patients with high-grade and/or high-stage disease. Metastatic restaging is generally not necessary for low-grade disease, where the risks of invasive and subsequent metastatic disease are negligible. There have been several approaches in the literature for bladder cancer which dictate follow-up based on tumor staging.<sup>70,71</sup> Since there are no established protocols for the upper urinary tract, we can adapt follow-up based on those findings. Physical examination, chest X-ray, and comprehensive metabolic panel with liver enzymes should be performed every 3 months for the first year, every 6 months for years 2 through 3, and annually for years 4 through 5. Subsequent years necessitate evaluation of the urothelium only. CT or MRI of the abdomen and pelvis should be performed every 6 months for the first 2 years and annually for years 3 through 5. Bone scans need only to be performed for elevated alkaline phosphatase or symptoms of bone pain.

### **Laparoscopic nephroureterectomy**

The gold standard therapy for people not at risk for renal failure and the risks of dialysis remains nephroureterectomy. Laparoscopy has greatly minimized the morbidity of the procedure with the avoidance of a multiple incisions or a single large incision to approach the entire urinary tract.

Laparoscopic nephroureterectomy has two distinct portions: removal of the kidney and complete ureterectomy with a cuff of bladder. The nephrectomy portion of the procedure can be confined to the kidney for lowgrade noninvasive lesions. Inclusion of Gerota's fascia with or without the adrenal should be considered for parenchymal invasive lesions. Multiple approaches to the nephrectomy portion of the procedure have been described, including transabdominal and retroperitoneal laparoscopic approaches and hand-assisted techniques. All these techniques are equally effective in cancer control and in minimizing

morbidity, provided that the principles of surgical oncology are applied. The choice of approach depends on patient factors as well as surgeon comfort. For hand-assisted techniques, one must consider placing the hand incision in a location that can be used for both specimen extraction and dissection of the distal ureter if necessary.

Multiple techniques for complete ureterectomy have been described to decrease morbidity. Such variations include transurethral resection of the distal ureter, total laparoscopic excision, and open removal via extravesical, transvesical, or combined approaches. Regardless of approach, an incision for intact extraction is always required for accurate pathologic staging.

An important factor with regards to TCC when performing distal ureterectomy is distal recurrence and the possibility of tumor seeding. Unlike renal cell carcinoma, where tumor implantation at extrarenal sites is a relatively uncommon event, there are multiple reports of seeding from TCC. Any approach that violates this closed system places the patient at risk for tumor seeding, especially with high-grade lesions. In addition, the propensity toward distal recurrence makes anything short of complete ureterectomy with a bladder cuff unacceptable, with the exception of rare, unusual circumstances. One should avoid approaches which involve removal of the distal ureter, leaving an 'open system' prior to control of the proximal ureter.

The authors' preference is to perform a standard laparoscopic radical nephrectomy with a dissection of the distal ureter as far distally as can safely be done. The incision for extractions is then placed strategically to complete removal of the distal ureter and bladder cuff. A low midline or Pfannenstiel incision is usually adequate if the ureteral dissection was carried out below the iliac vessels. In some cases where there is marked fibrosis of the periureteral tissue (prior surgery or multiple ureteroscopies), dissection below the iliac vessels is quite difficult. In such cases, a Gibson's incision provides exposure of the distal and mid ureter and can be used for specimen extraction. This approach allows flexibility in placing the incision and provides the patient with a procedure which is oncologically sound.

### *Results*

The first laparoscopic nephroureterectomy was performed in 1991 by Clayman and associates.<sup>72</sup> Since that time, the technical aspects and safety of laparoscopic procedures have been well established. There are multiple published series of laparoscopic nephroureterectomy.<sup>73-77</sup> Each varies with regard to approach (transperitoneal vs retroperitoneal), management of the distal ureter by open removal, transurethral resection 'pluck technique', and total laparoscopic management. As with other laparoscopic renal procedures, there is no clear-cut benefit of any one approach with regard to morbidity, cosmesis, or return to activity.

Hard and fast conclusions regarding cancer-related outcomes cannot be determined because there is only a single study with follow-up beyond 2 years.<sup>77</sup> The overall bladder recurrence rate of the combined studies is 16%, which is comparable to that of open nephroureterectomy. In the largest series, Shalhav and colleagues found that although the procedure took much longer than open nephroureterectomy, patients had a much shorter recovery time and equivalent outcomes with regard to bladder recurrence, metastatic

disease, and cancer-specific survival.<sup>77</sup> There were no reports of foreign bodies eroding into the bladder when the stapling device was used.

Local recurrence and port-site seeding are major concerns. There have been three reported instances of port-site seeding involving TCC of the upper urinary tract. Two of these cases were discovered after simple nephrectomy for presumed benign disease in which the principles of surgical oncology were inadvertently not followed.<sup>78,79</sup> In the third case, the proximal coil of a ureteral stent was seen protruding from the collecting system in the area of the tumor.<sup>80</sup> Another case was in an intended nephroureterectomy for high-grade disease (Barrett, pers comm). Although the potential for seeding exists, it does not appear any higher than that for the open surgical counterpart as long as good surgical principles are followed.

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## Laparoscopic retroperitoneal lymph node dissection for testicular tumors

Gunter Janetschek and Mohamed El Ghoneimy

Laparoscopic surgical techniques were first introduced to the field of urology a decade ago. Initial applications for benign diseases showed decreased postoperative pain, quicker convalescence, and improved cosmetic results as compared to open surgery. These successful results have provided the impetus for its introduction to the field of urologic oncology. In this chapter, we present the role of laparoscopic lymphadenectomy as a minimally invasive tool in the management of testicular tumors.

### **Pathology of testicular neoplasm**

Testicular cancer, although relatively rare, is the most common malignancy in men in the 15- to 35-year-old age group and evokes widespread interest for several reasons. The dramatic improvement in survival resulting from the combination of effective diagnostic techniques, improved tumor markers, effective multidrug chemotherapeutic regimens, and modifications of surgical technique has led to a decrease in patient mortality from more than 50% before 1970 to less than 5% in 1997.<sup>1</sup>

#### *Histologic classification of germ cell tumors*

Histologic classifications, grading systems, and staging evaluations have traditionally provided a major clinical basis for therapeutic decisions. There have been at least six major attempts since 1940 to classify germinal tumors. The World Health Organization (WHO) standardized pathologic criteria for diagnosis of testis cancer, which has gone a long way toward eliminating confusion associated with various histologic staging systems.<sup>2</sup> Germ cell tumors (GCTs) are composed of five basic cell types: seminoma, embryonal cell carcinoma, yolk sac tumor, teratoma, and choriocarcinoma. More than half of GCTs contain more than one cell type and are therefore known as mixed GCTs. Heterogeneity among germ cell neoplasms is an expected consequence of their pluripotential origin. Biochemical marker 'probes' can provide a means of delineating tumor heterogeneity, which may be useful in treatment selection.

Classification of germ cell neoplasms according to morphologic appearance is invaluable in treatment selection. The broad distinction between seminomas and

nonseminomas has been particularly important in determining management strategies for retroperitoneal lymph node metastasis.

In general, survival of patients with GCT is related to the stage at presentation and therefore to the amount of tumor burden as well as to the effectiveness of subsequent treatment. Patients who present with advanced disease (stage III) generally have a much poorer prognosis than do those with disease confined to the testis or those with regional nodal involvement only. Delay in diagnosis of 1–2 months or more is not uncommon in these patients and seems to be related directly to patient factors such as ignorance, denial, and fear as well as physician factors such as misdiagnosis.<sup>3</sup>

### *Patterns of spread of germ cell tumors*

The principles that underlie (the) modern surgical treatment of GCT of the testis are based on the fact that testis cancer spreads in a predictable and stepwise fashion, with the notable exception of choriocarcinoma. This will be explained later through the work of Weissbach and Boedefeld, who described templates that include practically all the primary landing sites of lymph node metastases and which were modified later by Hoeltl and colleagues.

### *Clinical staging*

A convenient division for staging systems is between patients with seminomas and those with nonseminomatous tumors. Patients with pure seminoma are usually staged by clinical means, whereas staging in patients with nonseminomatous germ cell tumors (NSGCTs) sometimes employs surgical techniques such as retroperitoneal lymph node dissection (RPLND) as well. The extent of staging is determined in part by decisions for therapy; for example, if surveillance protocols are to be considered, every effort should be made to exclude patients with any evidence of retroperitoneal disease. If retroperitoneal lymphadenectomy is likely to be elected as the primary treatment for low-stage, nonseminomatous tumors, efforts should be directed toward delineation of regional and nodal vs distant metastases.

### *Staging systems*

A variety of clinical staging systems have been advocated since the 1960s (Tables 39.1 and 39.2).

**Table 39.1** *Royal Marsden Hospital staging for testicular cancer*

| Stage | Definition  |
|-------|---|
| I     | No evidence of metastases                                 |
| M     | Rising serum markets with no other evidence of metastases |
| II    | Abdominal node metastases                                 |
| A     | <2 cm diameter  |



|     |   |
|-----|---|
| B   | 2–5 cm diameter                                   |
| C   | >5 cm diameter                                    |
| III | Supradiaphragmatic nodal metastases               |
| M   | Mediastinal                                       |
| N   | Supraclavicular, cervical, or axillary            |
| O   | No abdominal disease                              |
| IV  | Extralymphatic metastases                         |
| L1  | <3 lung metastases                                |
| L2  | >3 lung metastases all <2 cm in diameter          |
| L3  | >3 lung metastases, one or more >2 cm in diameter |
| H+  | Liver metastases                                  |
| Br+ | Brain metastases                                  |
| Bo+ | Bone metastases                                   |

*Source:* reproduced with permission from Hendry WE Testicular cancer. In: Kirby RS, Kirby MG, Farah RN, eds. Men's health. Oxford: Isis Medical Media, 1999:27.

In 1997, an internationally agreed-on consensus classification applicable to both seminoma and nonseminoma was published. The American Joint Committee on Cancer (AJCC) staging for GCTs is unique because, for the first time, a serum tumor marker category (S) is used to supplement the prognostic stages defined by anatomy alone. This tumor, nodes, and metastasis staging (TNMS) system should replace all prior staging systems and should, it is hoped, standardize patient reporting.<sup>4,5</sup>

The AJCC TNMS system subdivides stage I disease into stages Ia and Ib, depending on the T (tumor) stage, as well as into stage S (serum tumor markers), according to serum tumor marker levels; stage II is subdivided into stages IIa, IIb, and IIc, depending on volume of retroperitoneal lymph node involvement; and stage III is subdivided into stages IIIa, IIIb, and IIIc, according to the degree of metastatic involvement and serum tumor marker levels.

Removal of the testicular tumor is via an inguinal approach, the so-called *radical orchiectomy*, and remains the definitive procedure for pathologic diagnosis as well as for local treatment of testicular neoplasms. Transscrotal biopsy is to be avoided.

### *Imaging studies*

#### **Chest X-ray study**

Posteroanterior and lateral chest X-ray studies should be the initial radiographic procedures performed.

#### **Computed tomography**

Chest computed tomography (CT) scans are now routinely used, as they further increase the sensitivity for detection of pulmonary metastases. Abdominal CT scans have been advertised as being the most effective means to identify retroperitoneal lymph node involvement. CT scanning, however, is not sufficiently accurate to distinguish fibrosis,

teratoma, or malignancy by size criteria alone.<sup>6</sup> It also yields a good percentage of false-positive and at the same time false-negative results.

### Positron emission tomography

The use of positron emission tomography (PET) in the evaluation of retroperitoneal lymph nodes and radiographic abnormalities after chemotherapy in patients with testis cancer has been reported. No apparent advantage over CT scans has been demonstrated, mainly because neither PET nor CT has the ability to detect microscopic nodal disease.<sup>7,8</sup>

**Table 39.2** *AJCC TNMS staging system for testis cancer*<sup>4,5</sup>

#### *Primary tumor (T)*

|                 |   |
|-----------------|---|
| PT              | unknown   |
| PT <sub>0</sub> | no evidence of cancer   |
| PT <sub>1</sub> | confined to testis  |
| PT <sub>2</sub> | invades beyond tunica   |
| PT <sub>3</sub> | invades paratesticular structures (rete testis) and/or epididymis |
| PT <sub>4</sub> | invades cord structure  |
| P <sub>4</sub>  | invades scrotal structures  |

#### *Regional lymph nodes (N)*

##### *Clinical:*

|   |  |
|---|--|
| N   | cannot be assessed                         |
| NO  | no regional lymph node involvement         |
| N <sub>1</sub>                              | lymph node tissue <2 cm diameter           |
| N <sub>2</sub>                              | lymph node tissue 2–5 cm diameter          |
| N <sub>3</sub>                              | lymph node tissue > 5 cm diameter          |
| Pathologic PN <sub>0</sub> –PN <sub>4</sub> | same as above with pathologic confirmation |

#### *Distant metastases (M)*

|                |   |
|----------------|---|
| M <sub>0</sub> | no evidence of distant metastases         |
| M <sub>1</sub> | nonregional nodal or pulmonary metastases |
| M <sub>2</sub> | nonpulmonary visceral masses              |

#### *Serum tumor markers (S)*

| LDH           | hCG (m/u/ml) | AFP (ng/ml) |
|---------------|--------------|-------------|
| ≤normal       | ≤normal      | ≤normal     |
| < 1.5×normal  | <5000        | <1000       |
| 1.5–10×normal | 5000–50,000  | 1000–10,000 |
| >10×normal    | >50,000      | >10,000     |

AFP=alpha fetoprotein; hCG=human chorionic gonadotropin; LDH=lactic acid dehydrogenase

### Tumor markers

Germinal testis tumors are among a select group of neoplasms identified as producing so-called marker proteins that are relatively specific and readily measurable in minute quantities using highly sensitive radio—immunoassay technology (Table 39.3). The

study of biochemical marker substances, particularly alpha fetoprotein (AFP) and human chorionic gonadotropin (hCG), is clinically useful in the diagnosis, staging, and monitoring of treatment response in patients with germ cell neoplasms, and may be useful as a prognostic index. GCT markers belong to two main classes:

1. oncofetal substances associated with embryonic development (AFP and hCG) and
2. certain cellular enzymes, such as lactic acid dehydrogenase (LDH) and placental alkaline phosphatase (PLAP).

Tumor marker levels have to be evaluated before orchiectomy, especially when one is considering a surveillance protocol. Persistent serum tumor marker elevations after radical inguinal orchiectomy must be interpreted with caution to avoid unnecessary adjuvant treatment. Elevation of serum levels of AFP in patients with GCTs can be produced by liver dysfunction, and serum elevations of hCG can occur in hypogonadotropic patients. However, in general, persistently elevated tumor markers after orchiectomy reflect systemic metastases rather than tumor confined to retroperitoneal nodes, and for this reason chemotherapy is recommended for this subset of patients.

The rate of tumor marker decline relative to expected marker half-life after treatment has been proposed as a prognostic index. Patients whose values decline according to negative half-lives after treatment are more likely to be disease free than those whose marker decline is slower or whose markers never return to normal levels<sup>4,9</sup> (see Table 39.3).

## **Treatment options**

### *Non-seminomatous germ cell tumors*

#### **Clinical stage I**

Three treatment modalities are advocated by various urologists for the management of clinical stage I non-seminomatous testicular cancer: surveillance, risk-adapted chemotherapy, and retroperitoneal lymph node dissection.

Twenty-five to thirty percent of patients with clinical stage I have occult lymph node metastases, which cannot be diagnosed by the most sensitive imaging techniques available.<sup>10,11</sup> This group of patients will be at higher risk if surveillance strategy is followed, as they will be diagnosed later after the tumor has substantially increased in size, thereby requiring a higher dose of chemotherapy for treatment. Furthermore, as patient compliance is usually not perfect, some tumor-bearing patients might be lost during follow-up. Surveillance without prior lymph node dissection has a relapse rate of 19–40%<sup>12–14</sup> vs 5–10% for pathologic stage I testicular cancer after RPLND.<sup>15–18</sup> Moreover, the most serious drawback of surveillance is not only the high relapse rate but also the associated death rate of approximately 10% among those patients who do relapse.<sup>11</sup> The primary advantage of surveillance was the avoidance of RPLND and its attendant morbidity as, before the introduction of modified unilateral dissection and

nerve-sparing techniques, the majority of the patients suffered ejaculatory disturbances with resultant loss of fertility.<sup>19</sup>

Recently, risk-adapted chemotherapy has been introduced as a measure to overcome the above-mentioned problems.<sup>20</sup> However, there is no general consensus about risk factors and their clinical relevance, except for vascular invasion and embryonal carcinoma.<sup>21</sup> We have performed a retrospective analysis on 88 consecutive patients undergoing RPLND. Because the definition of risk factors varies greatly, the patients were evaluated using a highly specific risk factor (70% or more embryonal carcinoma together with vascular invasion) as an example of the many possibilities of calculating the risk. Even though the risk factor used was specific (present in 25% of the patients), 52% of patients who would have been considered candidates for chemotherapy did not have retroperitoneal tumors. On the other hand, 50% of patients with retroperitoneal tumors would have been considered low risk and left without treatment. Another staging study has also shown that 20% of patients with suspicious findings on CT actually have pathologic stage I disease.<sup>22</sup> These individuals might have unnecessarily been subjected to the side-effects of adjuvant chemotherapy: the acute ones (nausea, mucositis and nadir sepsis) as well as the long-term more morbid ones (pulmonary fibrosis and impaired spermatogenesis).<sup>23,24</sup>

RPLND is the only reliable method that permits the verification of small positive lymph nodes and the exclusion of false-negative ones. However, the morbidity of open RPLND is too high for a diagnostic procedure: the short-term morbidity of major intra-abdominal surgery

**Table 39.3** *Testicular tumor markers*<sup>5</sup>

| Tumor marker                                | Half-life<br>( $t_{1/2}$ ) | Clinical source of production  |
|---|----------------------------|--|
| Alpha fetoprotein                           | 5–7 days                   | Pure embryonal carcinoma<br>Terato carcinoma<br>Yolk sac tumor<br>Combined tumors                        |
| Beta-human chorionic gonadotropin           | 24–36 hours                | Syncytiotrophoblastic cells<br><br>Pure seminoma<br>Castration   |
| Lactic acid dehydrogenase (isoenzymes I–IV) | N/A                        | Common cellular enzyme found elevated when high tumor burden present (especially advanced pure seminoma) |
| Placental alkaline phosphatase              | N/A                        | Fetal isoenzyme elevated in advanced testicular cancer   |

and the long-term ones, which are much less tolerated because of loss of antegrade ejaculation and a lifelong scar that impairs the quality of life of a usually young patient.

Since knowledge of the definite lymph node status is a prerequisite for adequate stage-adapted treatment, RPLND is retained as a diagnostic and in a way therapeutic tool, its morbidity being substantially reduced by the use of laparoscopy.

Our recent data, as well as the data from other centers, will show that laparoscopy shares the same efficacy as open RPLND. Relapse rates after open RPLND alone are as

high as 8–29% for stage IIa tumors<sup>25,26</sup> and 34–55% for stage IIb tumors.<sup>26,27</sup> This rate falls to as low as 0–1% if two cycles of adjuvant chemotherapy are given.<sup>27,28</sup> Laparoscopic RPLND, thereby, reduces the high morbidity of the combination of open RPLND and adjuvant chemotherapy in node-positive patients.

### *Clinical stage II*

Neither retroperitoneal lymphadenectomy<sup>25–27,29</sup> nor chemotherapy<sup>30,31</sup> alone can be expected to be curative in all patients in this stage. A combination of both is expected to achieve the most effective results. Most urologists prefer the strategy of primary chemotherapy followed by RPLND for residual masses. In this case, RPLND is performed in a diagnostic intent, i.e. to exclude the residual mass containing active tumor, but sometimes can be curative, i.e. if a mature teratoma is found and removed. Again, the advantage of laparoscopy here rises by reducing the (double) morbidity of chemotherapy and open surgery. In an attempt to further reduce the morbidity of this combined treatment, we have reduced the dose of chemotherapy to two cycles for stage IIb, which is obviously the minimum dose required for complete tumor control.<sup>32</sup> However, this approach is experimental at present, which makes the evaluation of the effect of chemotherapy by laparoscopic RPLND mandatory in each patient. RPLND can be performed as a first step in a therapeutic intent. In this case, it has to be done bilaterally to remove not only the primary landing site but also all possible sites of tumor spread. By laparoscopy, bilateral RPLND is only feasible as a staged procedure, which decreases efficiency and increases the morbidity. Other studies have found laparoscopic RPLND for residual masses to be not recommendable, owing to the intense desmoplasia in the vicinity of the great vessels after chemotherapy,<sup>33</sup> but our results have shown it to be technically feasible not only in stage IIb but also in stage He. However, in the latter stage, the risk of contralateral tumor spread is high and, as laparoscopy allows for unilateral dissection only, we have now restricted it to stage IIb.<sup>32,34</sup>

### *Seminoma*

Since the morbidity of carboplatinum monotherapy is low and its efficacy is very high, we feel there is no place for laparoscopy in the management of stage I seminoma.<sup>35</sup> The only exception we consider is the removal of residual masses after chemotherapy.

## **Technique**

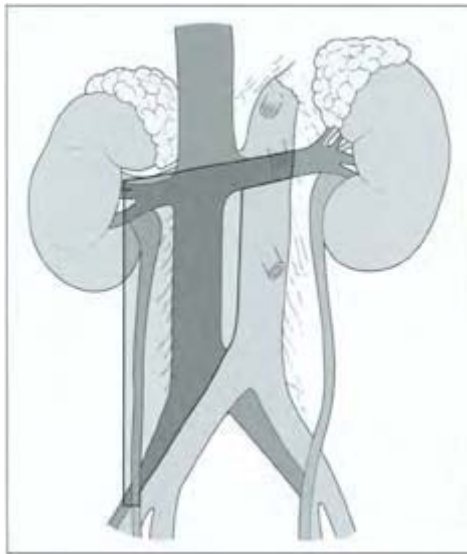
### *Preoperative measures*

Bowel preparation, including a clear liquid diet and oral laxatives, is performed day 1 preoperatively. All patients receive low-dose antibiotic coverage. Typing and crossmatching are performed for two units of blood. Preoperative preparation now also includes a low-fat diet for 1 week that is continued 2 weeks postoperatively so as to prevent chylous ascites, which was observed in some patients after postchemotherapy laparoscopic RPLND. We have not seen this complication since.

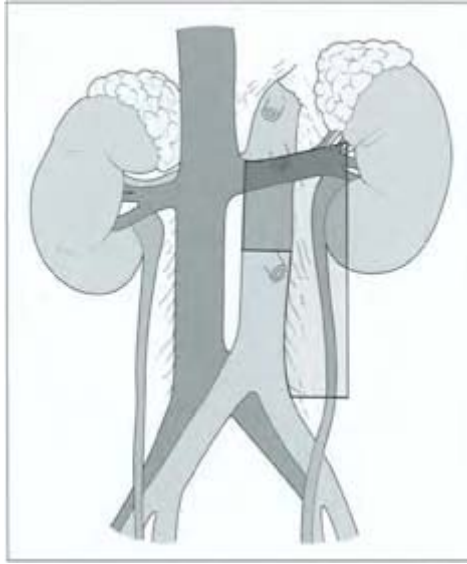
*Template*

Weissbach and Boedefeld have described templates that include practically all the primary landing sites of lymph node metastases.<sup>36</sup> If all the metastatic tissue is resected within these templates, there is only minimal risk of metastases to be overlooked. The templates for the left and right sides differ substantially; only the templates for right-sided tumors include the interaortocaval tissues (Figures 39.1 and 39.2).

However, there is still some controversy as to whether to remove the tissues behind the lumbar vessels, the vena cava, and the aorta. There is currently no study available investigating whether this area is among the primary landing sites of lymph node metastases. We have developed a laparoscopic split and roll technique that enables transection of all lumbar vessels and enables us to perform the same radical dissection as with open surgery. Meanwhile, we have investigated the primary landing sites as regards their ventrodorsal location. All solitary metastases, and at least, in one patient, multiple metastases, were detected ventral to the lumbar vessels. Therefore, it can be concluded that the primary landing sites are invariably located ventrally, whereas dorsal metastases result from further tumor spread.<sup>37</sup> Consequently, we no longer routinely transect the lumbar vessels to remove the tissues behind them, as it is not required in diagnostic RPLND for clinical stage I tumors. This makes the laparoscopic procedure considerably easier, faster, and safer.



**Figure 39.1** Template for right-sided dissection.



**Figure 39.2** Template for left-sided dissection.

The same procedure is performed in clinical stage II disease following chemotherapy. All tissue in which tumor was detected before chemotherapy is removed and the ipsilateral template is dissected in the same fashion as in clinical stage I disease.

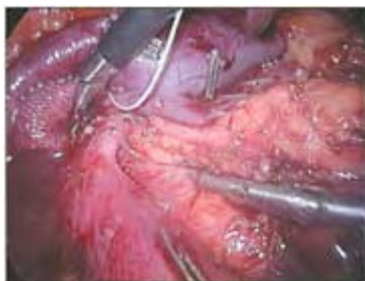
### *Equipment*

The following tools have proved useful additions to the standard laparoscopic equipment. We exclusively use a 3-chip video camera and a 30° laparoscope. The laparoscope is held and maneuvered by a robotic arm (Computer motion, Inc., Santa Barbara, California). This robot is used to replace one assisting surgeon and has the advantage of providing stable video images even in lengthy procedures. Insufflation with a high flow rate has proved helpful because it prevents the pneumoperitoneum from collapsing during suction.

A small surgical sponge held with an atraumatic grasper is used for retraction, dissection, and hemostasis (Figure 39.3). A right-angled dissector (Aesculap; Karl Storz, Tuttlingen, Germany) is applied for dissection of the vessels. We prefer the use of reusable clips because their small branches allow for more precise placement of the clips.

*Operative technique***Clinical stage I: right side**

The patient is placed on the operating table with the right side elevated 45° upwards so that the patient can be brought into a supine or lateral decubitus position by rotating the table. In addition the table is flexed at the umbilicus. If necessary, the Trendelenburg or antiTrendelenburg position is used. The patient is secured to the table.



**Figure 39.3** Blunt dissection and retraction with sponge.

A Veress needle is used for the initial stab incision to create the pneumoperitoneum, whereas the Hasson cannula is preserved for patients who have previously undergone abdominal surgery. Only 10 mm trocars are used. The first trocar for the laparoscope is placed at the site of the umbilicus. Two secondary trocars for the surgeon are placed at the lateral edge of the rectus muscle, approximately 8 cm above and below the umbilicus. One more trocar is positioned in the anterior axillary line to facilitate retraction.

Wide access to the retroperitoneum is a prerequisite for laparoscopic RPLND. Excellent access can be gained by wide dissection of the right colon and the duodenum in the plane of Toldt. As a first step, the peritoneum is incised along the line of Toldt from the cecum to the right colic flexure. This incision is then carried cephalad parallel to the transverse colon and lateral to the duodenum along the vena cava all the way up to the hepatoduodenal ligament. Caudally, the incision is carried along the spermatic vessels down to the internal inguinal ring. Next, the colon, the duodenum, and the head of the pancreas are reflected medially until the anterior surface of the vena cava, the aorta, and the origin of the left renal vein are exposed.

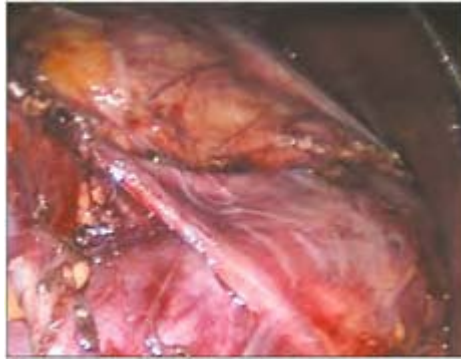
At this point, the entire template described by Weissbach and Boedefeld for right-sided tumors is accessible. This template includes the interaortocaval lymph nodes, the preaortic tissue (between the left renal vein and the inferior mesenteric artery), and all the tissue ventral and lateral to the vena cava and the right iliac vessels (between the renal vessels and the crossing of the ureter with the iliac vessels). The lateral limit of the template is the ureter. As mentioned previously, the tissues behind the lumbar vessels and



the vena cava are no longer removed. The spermatic vein is then dissected along its entire course, starting from the internal inguinal ring.

Special care must be taken while dissecting its insertion into the vena cava, because at this point the vein is easily ruptured. Cranially, the spermatic artery takes a separate course; it is clipped and transected at its crossing with the vena cava, whereas its origin from the aorta is approached later (Figure 39.4).

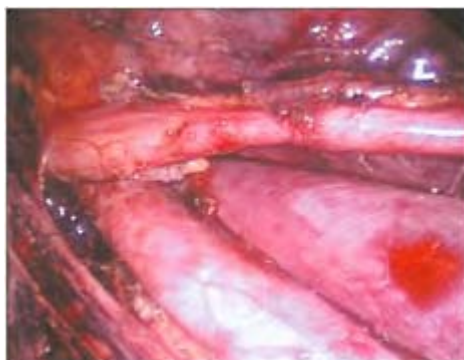
Next, the lymphatic tissue overlying the vena cava is split open cranially to caudally and its anterior and lateral surfaces are dissected free. Both renal veins are freed from surrounding lymphatic tissue. It is important to dissect the lower border of the left renal vein at this point of the procedure. When dissecting the interaortocaval package from caudal in a cephalad direction, the left renal vein can be easily injured if it is not clearly visible. The lymphatic tissue overlying the common iliac artery is incised up to the bifurcation and further to the origin of the inferior mesenteric artery. In this area, the lymphatic tissue is very dense and care must be taken not to injure the mesenteric artery. Cephalad to the artery, the lymphatic tissue is split along the left border of the aorta so that the ventral surface



**Figure 39.4** Right RPLND: spermatic artery and vein; the artery crosses the vena cava.

of the aorta is completely freed. The spermatic artery is now clipped and transected at its origin from the aorta. When dissecting the cranial portions of the template, the liver has to be retracted with a fan retractor. Now, the right renal artery can be identified as it courses above the interaortocaval space, and the cranial border of the dissection is well delineated. The dissection is carried down to the lumbar vessels and the interaortocaval package is removed step by step.

The ureter, which defines the lateral border of the dissection, is usually identified during excision of the spermatic vessels. It is separated from the nodal package down to its crossing with the iliac artery (Figure 39.5). This point delineates the distal border of the dissection, and the lymph node package is clipped and transected.



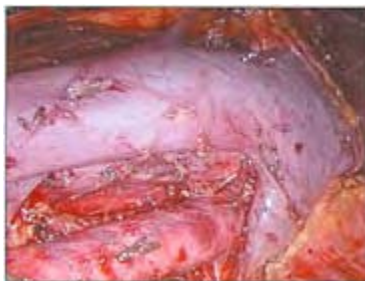
**Figure 39.5** Right RPLND: lower limit of dissection; ureter crossing common iliac artery and vein.

From here, the lymph nodes are dissected free in a cephalad direction. The lumbar veins are exposed, but they are transected in exceptional cases only to facilitate removal of the lymph nodes (Figure 39.6). Cranially, the ureter enters Gerota's fascia, which can also be differentiated clearly from the lymphatic tissue. In addition to the right renal vein, the right renal artery is exposed lateral to the vena cava, which delineates the cranial border of the dissection (Figures 39.7 and 39.8).

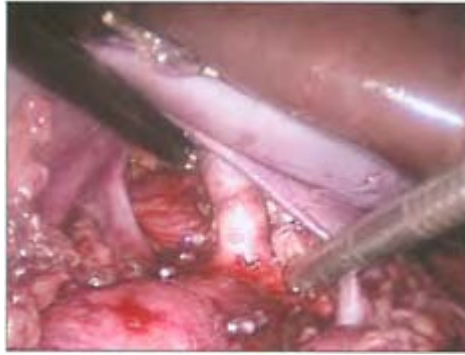
Now, the nodal package is completely free and can be removed inside a specimen retrieval bag. A drain is not required. Finally, the colon and the duodenum are returned to their anatomic positions and secured with one suture, which is tied extracorporeally.

#### Left side

The patient is in a right decubitus position. The trocars are placed as for right-sided tumors but in a mirror image



**Figure 39.6** Right RPLND: interaortocaval space.



**Figure 39.7** Right RPLND: renal artery and vein.

array. Usually three or four 10 mm trocars will suffice, because the bowel has to be retracted in rare cases only.

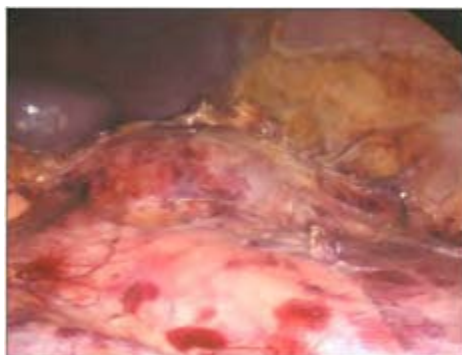
The peritoneum is incised along the line of Toldt from the left colonic flexure to the pelvic brim and distally along the spermatic vein to the internal inguinal ring. It is essential also to incise the splenocolic ligament.

The dissection of the colon must be continued until the anterior surface of the aorta is exposed completely in the plane of Toldt. Normally, the colon falls away from the operative site because of gravity, and a retractor is required only in a few exceptional cases (Figure 39.9).

Then, the spermatic vein is dissected free along its entire course from the internal inguinal ring to its opening into the renal vein and removed (Figure 39.10). The ureter, which defines the lateral border of the template, is identified and separated from the lymphatic tissue. Care must be taken to preserve the connective tissue that provides the blood supply of the ureter. Now, the renal vein can be freed completely. Next, the lymphatic tissue overlying the common iliac artery is split open. The dissection is started



**Figure 39.8** Right RPLND: operative field lateral to vena cava after completion of dissection.



**Figure 39.9** Left RPLND: plane of Toldt after colon reflection.



**Figure 39.10** Left RPLND: left renal vein with the opening of spermatic vein.

at the crossing of the artery with the ureter, which delineates the distal border of the template. From there, the dissection is continued cephalad. The inferior mesenteric artery is circumvented on the left and preserved. Directly above the mesenteric artery, the dissection is continued along the medial border of the aorta up to the level of the renal vein, which has been identified before.

The spermatic artery is secured with clips at its origin from the aorta and transected. The lateral surface of the aorta is dissected down to the origin of the lumbar arteries. Next, the lumbar vein, which passes caudal to the left renal artery, is approached as it enters the renal vein and transected between clips. This provides access to the renal artery, which lies directly underneath (Figure 39.11). As a last step, the lumbar vessels are separated from the lymphatic tissue to the point at which they disappear in the layer between the spine and the psoas muscle.



**Figure 39.11** Left RPLND: left renal artery and vein (cranial limit of dissection).

Directly lateral to that point, the sympathetic chain is encountered. The postganglionic fibers, although readily identified in most cases, are not preserved. Now, the nodal package is completely free and can be retrieved (Figure 39.12). Finally, the colon is returned to its normal anatomic position and secured in place with one extracorporeally tied suture.

*Laparoscopic retroperitoneal lymph node dissection for stage II after chemotherapy*

Unilateral RPLND is performed within the same template as is used for clinical stage I disease. Bilateral RPLND is not attempted; in all of our 58 patients, the residual tumor was located within the unilateral template. Displacement of the bowel was feasible in all cases, although chemotherapy rendered identification of the tissue layers more difficult. Mature teratoma is usually well delineated, whereas tumorfree residuals after embryonal carcinoma may be tightly adherent to the surrounding structures (Figure 39.13). This is particularly true for the vena cava. Small venous branches draining the tumor have to be meticulously dissected before they are clipped and transected.

**Technique of dissection and hemostasis**

The most useful tools for achieving bloodless dissection and adequate hemostasis are bipolar coagulation forceps and the harmonic scalpel (Ethicon, Endo-surgery, Cincinnati, Ohio). Ever since the authors have been using these tools, dissection has become easier, safer, and faster. A small clamp for bipolar coagulation (Johnson and Johnson, New Brunswick, New Jersey) allows for meticulous dissection



**Figure 39.12** Left RPLND: operative field after completion of dissection.



**Figure 39.13** Right RPLND: residual mass after chemotherapy overlying the vena cava.

of delicate structures, whereas broader bipolar forceps provide highly efficient hemostasis. In our hands, these tools have proved very efficient.

In open surgery, acute bleeding can be stopped instantaneously with the index finger of the surgeon. In laparoscopy, a small surgical sponge that is held with an atraumatic grasper can be used to substitute for the surgeon's finger. Once the bleeding has been stopped with this technique, the surgeon needs not act in a hurry but has plenty of time to undertake the necessary steps. Furthermore, our animal studies and clinical experience have shown that most venous bleedings, including those resulting from small leaks in the vena cava, can be stopped with the help of the fibrin glue (Tisseel; Baxter-Immuno, Deerfield, Illinois). A special laparoscopic applicator is available (from the manufacturer) with two separate channels for the two components of fibrin glue. The edges of larger defects are approximated with a grasper or clips and then sealed with fibrin glue. In addition, a strip of oxidized regenerated cellulose or other hemostatic agents can be used to enhance the tightness of the repair. Using these hemostatic techniques, only 3 out of

122 laparoscopic RPLNDs had to be converted to open surgery. No late bleeding was observed.

## Results

Between August 1992 and October 2002, 159 consecutive patients underwent laparoscopic RPLND. No patients were excluded because of body habitus or previous operations (Tables 39.4 and 39.5).

### *Stage I*

RPLND was performed for 101 patients with clinical stage I testicular tumor. Mean age was 29.9 years old (16–51). In 64 patients, the tumor was located on the right side and in 37 on the left side. Patient selection was not based on assessment of risk factors or histologic findings.

### Surgical efficacy

Laparoscopy is a technically challenging procedure, that requires a steep learning curve. However, once this obstacle is overcome, its results are comparable to and sometimes even better than open surgery. This can be demonstrated by our operative time, which fell from an average of 276 min to 217 min on exclusion of the first 30 patients. This time is now shorter than the mean operative time reported for open RPLND<sup>40,41</sup> and comparable to operative

**Table 39.4** *Demographic and perioperative data for laparoscopic RPLND*

|                  | Clinical stage I   | Stage II after chemotherapy                   |
|------------------|--|---|
| Patients No.     | 101  | 58  |
| Mean age (years) | 29.9   | 29.1  |
| Tumor side       | Right: 64 Left: 37   | Right: 32 Left: 26                            |
| Operative time   | Overall: 276 min (140–360) After 1st 30 cases: 217 min (140–300) | I Ib: 216 min (135–300) He: 281 min (145–360) |
| Blood loss       | 144 ml (10–470)  | 165 ml (20–350)                               |
| Conversion rate  | 3/101 (3%)   | No conversion                                 |
| Hospital stay    | 3.6 days (2–8)   | 3.8 days (3–10 days)                          |

**Table 39.5** *Outcome data for laparoscopic RPLND*

|                 | Clinical stage I | Stage II after chemotherapy |
|-----------------|------------------|-----------------------------|
| Mean follow-up  | 47 months (4–97) | 38 months (3–73)            |
| Patients No.    | 96/101           | 58/58                       |
| No. of relapses | 2                | None                        |

Antegrade ejaculation 98/98 (100%)    56/58 (96.5%)

time in other series.<sup>38,39</sup> Mean blood loss was 144 ml (range 10–470), not including 2600 ml in a converted patient with horseshoe kidney. We had three conversions: one due to injury of a small aortic branch, another due to injury of a renal vein in a horseshoe kidney, and the third due to injury of a left renal vein ventral to the aorta (conversion rate 3%). Four other minor intraoperative complications were encountered, including vena caval, renal, and lumbar vein injury. All were controlled laparoscopically with either clips or fibrin glue; a left renal vein injury was controlled via laparoscopic suturing. Few minor complications occurred postoperatively, including three asymptomatic lymphoceles, a transient irritation of the genitofemoral nerve, and a spontaneously resolving retroperitoneal hematoma. Other groups have reported ureteral stenosis following ureteric stenting, which was abandoned later on, as well as the need for temporary ureteric drainage in some cases.<sup>38</sup> Mean postoperative hospitalization was 3.6 (2–8 days).

### **Oncologic efficacy**

Histologic findings were positive in 25 of the 101 patients (25%). Some groups have reported the number of resected lymph nodes but this doesn't appear practical, since to our knowledge there are no data to indicate how many lymph nodes a specimen must contain to prove the completeness of the dissection in a given template.

Follow-up data are available on 96 of our 101 patients; 5 patients were lost during follow-up. Of 96 pathologic stage I patients on a mean follow-up of 47 months, 2 relapses were reported (see Table 39.5). One retroperitoneal recurrence occurred on the contralateral side outside the surgical field. Further investigations revealed that the tumor in the primary landing site had been removed at surgery but was missed on histologic examination. This patient was cured with two cycles of chemotherapy and contralateral laparoscopic RPLND. Another patient developed lung recurrence during follow-up. No further relapses occurred, which clearly demonstrates the oncologic efficacy of the procedure. Rassweiler et al.<sup>38</sup> and Gerber et al.<sup>39</sup> also reported pulmonary relapses in 4 cases, but no retroperitoneal relapses.

The rate of retroperitoneal relapse after open RPLND was reported to be 6.8% in 88 clinical stage I patients; 37 of the 88 patients had pathologic stage I lesions.<sup>40</sup> By comparison, the relapse rate in our series is extraordinarily low, a fact that cannot be explained. Nevertheless, it is tempting to speculate that at least some of the recurrences in the literature may be due to false-negative findings on histologic examination.

The mean follow-up in 25 clinical stage I pathologic stage II patients who received two cycles of adjuvant chemotherapy (all except 1 patient with mature teratoma) is currently 47 months. Over this time period, no relapse has been seen.

### *Stage II after chemotherapy*

Between February 1995 and October 2002, 58 patients with clinical stage II underwent RPLND (42 stage IIb and 16 stage IIc). The mean age was 29.1 years old (15–56). The procedure was performed on the right side in 32 patients and on the left in 26. The mean



operative time was 234 min (135–360) and the mean blood loss was 165 ml (20–350). No conversion occurred and the spectrum of complications was almost the same as in stage I patients with a higher incidence of chylous ascites in stage II. Postoperative hospital stay averaged 3.8 days (3–10 days).

Histologic analysis of the specimens revealed necrosis in 36 patients, mature teratoma in 20 patients, active tumor in 1 patient and seminoma in 1 patient (Table 39.6). To date, this was our only seminoma case for which RPLND was performed. The patient had a residual tumor 6 cm in size following three cycles of chemotherapy (20% of the original tumor size). A PET scan showed no reduction in size between the second and third course and no signs of vital tumor. RPLND was performed on the left side; the procedure was quite difficult owing to a large tumor mass and numerous venous interconnections. Histology revealed small foci of a vital tumor. On a mean

**Table 39.6** *Postoperative pathology for residual mass (laparoscopic resection)*

|  |                  |
|--|------------------|
| Stage II after chemotherapy: postoperative pathology | No. of patients  |
| Total number   | 58 patients      |
| Necrosis   | 36 cases (62%)   |
| Mature teratoma                                      | 20 cases (34.5%) |
| Active tumor   | 1 case (1.7%)    |
| Seminoma   | 1 case (1.7%)    |

follow-up of 38 months (3–73), no relapse was detected in any of these 58 patients.

#### *Antegrade ejaculation*

Loss of antegrade ejaculation (see Table 39.5) is the major morbidity encountered after RPLND. This drawback can be overcome either by performing a template dissection, as described by Weissbach and Boedefeld<sup>36</sup> or by nerve sparing RPLND.<sup>14</sup> The template dissection, although downscaling the operative field, maintains acceptable sensitivity and, more importantly doesn't increase relapse rate. We have followed this strategy in our work, and in 98 of our stage I patients, antegrade ejaculation rate was 100% (3 patients were lost during follow-up). In stage II patients, antegrade ejaculation was preserved in 56 out of 58 patients.

With the introduction of nerve-sparing RPLND, Donohue was able to improve the ejaculation rate from

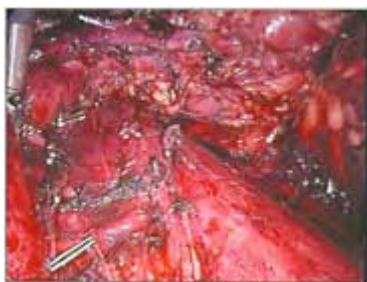


**Figure 39.14** Seminoma: residual mass after chemotherapy, overlying the aorta.

70 to almost 100%. Donohue did not only introduce nerve-sparing dissection but also simultaneously limited the dissection to the unilateral template.<sup>15,19</sup> It has been known since 1964 that destruction of the sympathetic chain on one side doesn't result in aspermia as long as the contralateral side is intact.<sup>42</sup> Therefore, nerve-sparing, in addition to a unilateral dissection, is not necessary and cannot improve the already good results. Recently, Peschel et al published the results of laparoscopic nerve sparing RPLND in 5 patients, showing an operative time of 3.2 hours average, a blood loss of 66 ml, and a hospital stay of 3.7 days (results comparable to the standard procedure). This required meticulous dissection and identification of the sympathetic chain and the postganglionic fibers in the retrocaval, the interaortocaval, and the para-aortic regions. Although, as we mentioned earlier, antegrade ejaculation is routinely preserved when a nerve-sparing dissection is limited to a unilateral template, the development of a unilateral laparoscopic nerve-sparing technique is a step towards bilateral laparoscopic dissection.<sup>43</sup>

### *Quality of life*

A major issue to be considered when comparing various treatment modalities is the patient's quality of life thereafter. Thus, a quality of life study has been performed in coordination with a psychiatric group at our center. A questionnaire was distributed to 119 patients and completed by personal interviews with 118 (the open group consisted of 53 patients and the laparoscopic group 59). The questionnaire included questions about the patient's satisfaction with the information about the disease, and his experience of treatment and its sideeffects. Patients were asked about the time it took them



**Figure 39.15** Seminoma: operative field after excision of residual mass (lateral edge of aorta, lumbar artery, and psoas muscle).

until they were able to perform moderate physical exercise, return to normal activities, and were free of symptoms. Other questions—regarding sexual activity, whether the patient felt lovable, experienced any problems in his partnership, psyche, or social life, and whether he was anxious about losing his job or had emotional problems associated with the loss of testicle or the RPLND procedure—were also addressed. Surprisingly, the patients better tolerated not only laparoscopic RPLND but also open RPLND rather than chemotherapy. Open RPLND was found to impair the quality of life more than laparoscopic RPLND. There is not a single item where open RPLND was superior to laparoscopy. The patients who participated in the study preferred RPLND to all other treatment modalities.<sup>44</sup>

#### *Cost-effectiveness*

Although costs are not a primary issue, they have to be taken in consideration. In our series, the surgical procedure itself was found to be less expensive if done by the open rather than by the laparoscopic approach, but adding the hospital stay to the surgical costs brings the latter down in the case of laparoscopy so that the total hospital costs in both groups are almost equal. Another factor that has not been taken into account in most studies is the time to convalescence, especially considering that most of our patients are young productive individuals. If this factor were to be added, laparoscopy would definitely be the clear winner.<sup>32</sup>

#### *Extra peritoneal approach*

Two centers have described an extraperitoneal approach for laparoscopic RPLND. One group strongly supports the procedure, arguing that it is more safe to the bowel and other viscera, and suggesting that it provides better access to the retrovascular areas, thereby facilitating nervesparing dissection.<sup>45</sup> However, based on our experience, the risk of bowel injury is minor during transperitoneal RPLND, as it is totally out of the operative field. On the other hand, access to the retrovascular area is not really required, as it is not

included in the template dissection, since lymph node metastases were found to be exclusively ventral to the lumbar vessels. In addition, we feel that the transperitoneal route gives a better access to the interaortocaval area, for the right-side RPLND. Although this first group did not report any incidence of lymphocele, it is expected to occur once a larger group of patients is evaluated.<sup>32</sup> In short, we are not convinced that retroperitoneoscopy offers any major advantage over the transperitoneal approach.

### Summary

In our hands, laparoscopic RPLND has demonstrated its surgical and oncologic efficacy. The morbidity and the complication rate are low. Adherence to the templates described above allows for preservation of antegrade ejaculation in virtually all patients. It is a difficult procedure indeed, but once the long and steep learning curve has been overcome, operative times are equal to or even shorter than those of open surgery. Thereafter, the costs will be in the range of open surgery. The recurrence rate of laparoscopic RPLND is at least as low and survival is equal to that of open surgery and chemotherapy. Patient satisfaction, however, is clearly higher with laparoscopic RPLND, which the authors demonstrated in a recent extensive quality of life study.

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## Carcinoma of the prostate—diagnosis and staging

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Prostate cancer is the most commonly diagnosed malignancy and the second leading cause of cancer death in the male population over the age of 40 in the United States. Approximately 198,000 American men were diagnosed with prostate cancer, and almost 32,000 men died from the disease in the year 2001.<sup>1</sup> Adenocarcinoma of the prostate most frequently arises in the periphery of the gland, thus making it more easily detected by digital rectal examination (DRE). The predisposition for prostate cancer to originate from the peripheral zone increases the likelihood that patients with early stages of the disease will remain asymptomatic. The presence of obstructive or irritative voiding symptoms rarely suggests locally advanced or metastatic disease resulting from growth of the cancer into the urethra or bladder neck and is often the result of benign prostatic hyperplasia (BPH). Other less common findings that may be elicited from the history of a patient with more advanced disease include hematospermia (rare), decreased ejaculate volume, impotence, bone pain, anemia, and lower extremity edema.<sup>2</sup>

### Diagnosis

In the past, diagnosis of prostate cancer was primarily accomplished by obtaining a thorough history of the patient and from physical examination findings. Over the last two decades, there has been increased utilization of serum prostate-specific antigen (PSA) to aid in diagnosis in addition to its use for monitoring progression following definitive therapy. The so-called 'PSA era' and changes in prostate cancer incidence and mortality have been associated with widespread acceptance of PSA testing by clinicians.<sup>3,4</sup> Perhaps the most compelling evidence that suggests a benefit from early detection of prostate cancer using PSA is the observation of a decline in prostate cancer mortality rates to below those which existed prior to its diagnostic use. In 1997, prostate cancer mortality rates in the United States for men 60–79 years of age were the lowest in almost 50 years, and for white men less than 85 years of age prostate cancer mortality rates decreased to levels below those observed in 1986 (the year PSA testing was approved).<sup>4</sup> The reduction in overall mortality may be attributed to an increased number of high-grade cancers being detected before metastasis. A concomitant decrease in the incidence of distant-stage disease at an annual rate of almost 18% over the past decade also supports the argument that PSA testing has resulted in lower prostate cancer mortality.<sup>3,5</sup> Further evidence supporting the beneficial impact of early disease detection with PSA was provided in a unique natural study that compared prostate cancer mortality in Tyrol, Austria, where

PSA testing was introduced at no charge, with the rest of Austria, where it was not introduced.<sup>6</sup> The trends in prostate cancer mortality rates since 1993 were significantly lower in Tyrol compared to the rest of Austria. The combination of DRE and serum PSA represents the most useful initial diagnostic tool for the assessment of prostate cancer at the present time.<sup>7-9</sup>

### *Digital rectal examination*

DRE is considered to be an essential component of the urologic evaluation and has been the primary method for assessment of the prostate. An abnormal DRE, regardless of PSA level, warrants further work-up, especially in men with risk factors for prostate cancer (i.e. older age, family history, race, elevated PSA, symptoms). The positive predictive value of DRE has been shown to be dependent upon age, race, and PSA level.<sup>10,11</sup> Prostate biopsy is recommended for all patients who have an abnormal DRE, regardless of serum PSA, since up to 25% of men with prostate cancer will have PSA levels <4.0 ng/ml.<sup>2</sup> The reproducibility of DRE is limited even among experienced clinicians, and a significant number of cancers may still be missed.<sup>12</sup> This variability may result in detection of cancer at a more advanced stage. In fact, there is often a significant amount of clinical understaging by DRE compared with pathologic stages of radical prostatectomy specimens.<sup>13-15</sup> Over 50% of patients in screened and unscreened populations were found to have more pathologically advanced disease when their prostate cancer was detected by DRE.<sup>16,17</sup> The sensitivity and specificity for detection of organ-confined prostate cancer by DRE alone have been estimated to be approximately 52% and 81%, respectively.<sup>18</sup>

### *Prostate-specific antigen*

PSA is a 33 kDa serine protease that facilitates liquefaction of the seminal coagulum shortly following ejaculation.<sup>19,20</sup> The majority of PSA found in serum is complexed either to alpha1-antichymotrypsin (ACT) or alpha<sub>2</sub>-macroglobulin (MG).<sup>21-23</sup> The most detectable form of PSA in serum (65–90%) is bound to ACT. Approximately 10–35% of detectable PSA found in the circulation exists either as unbound or free.<sup>22,23</sup> Free PSA lacks proteolytic activity and circulates as an inactive molecule. Protease complexes are typically metabolized in the liver. The large size of complexed PSA may prevent filtration at the level of the glomerulus.<sup>24</sup>

Secretion of PSA normally occurs via the prostatic ductal epithelium in mg/ml concentrations and it is found in low serum concentrations (ng/ml). Changes in prostate tissue architecture during tumorigenesis may result in secretion of PSA into blind-ending ducts, thereby causing an increase in leakage into the circulation and raising serum concentrations. Diffusion of PSA into the prostatic tissue and an increase in serum PSA levels may also occur in benign conditions (e.g. BPH, prostatitis) or after manipulation (e.g. prostate massage, biopsy).<sup>25-28</sup> The presence of prostatic disease (benign or malignant) remains the most important factor influencing serum PSA levels. Therefore, elevation of PSA is not necessarily specific for cancer.<sup>2</sup>

Administration of a 5-alpha reductase inhibitor such as finasteride (Proscar) for the treatment of BPH has been shown to decrease PSA levels by as much as 50% after 12



months.<sup>29</sup> It is recommended that a baseline PSA level be obtained prior to initiation of finasteride in men who undergo treatment for BPH. Interpretation of PSA levels should always take into consideration the presence of benign prostatic disease, prostatitis, and manipulation. Failure of PSA to decrease by 50% or a rise in PSA while taking finasteride should raise suspicion of the existence of occult prostate cancer.<sup>2</sup>

### **Clinical utility of prostate-specific antigen**

Comparison of the various methods for prostate cancer detection has demonstrated that PSA elevation has the highest positive predictive value for the presence of malignancy.<sup>2</sup> A higher percentage of patients will have cancer found at biopsy in the presence of a markedly elevated serum PSA (>10.0 ng/ml) compared to an abnormal DRE or transrectal ultrasound (TRUS).<sup>7,30</sup> The use of PSA has been shown to increase the predictive value of DRE for cancer detection.<sup>10,31,32</sup> Therefore, combined use of DRE and PSA for assessment of prostate cancer risk remains the most effective method for early detection of malignancy.<sup>2</sup> Recent results have shown little difference in the overall characteristics of prostate cancer cases detected by utilizing a PSA cutoff of 3.0 ng/ml compared to cases detected with a regimen based on PSA, DRE, and TRUS.<sup>33</sup> This indicates a possible role for PSA measurement alone as a baseline screening test for prostate cancer.

Various PSA threshold levels have been proposed above which further evaluation (i.e. biopsy) is warranted to rule out cancer. This area remains highly controversial, but the most commonly used threshold value is a PSA of 4.0 ng/ ml.<sup>34,35</sup> Age- and race-specific PSA ranges have been previously established (Table 40.1).<sup>36,37</sup> Threshold PSA levels for detection of approximately 95% of prostate cancers among men aged 40–50 years are lower than 4.0 ng/ ml. For Caucasian and African-American men 50–69 years of age, threshold PSA levels are very close to 4.0 ng/ml. It has been suggested that a PSA threshold of 4.0 ng/ml should be utilized, regardless of age or race.<sup>38</sup> African-American men may have higher PSA levels overall compared to Caucasian males, and race-specific threshold levels have been established at higher levels for this population. Utilization of a PSA threshold of 4.0 ng/ml, regardless of age or race, may lead to earlier disease diagnosis and increase the chance for curative intervention, particularly for African-Americans, since this population often has more aggressive disease at the time of presentation.<sup>38</sup> While the utility of PSA screening remains controversial, an unvalidated strategy of PSA testing (with a threshold of 4.0 ng/ml) at ages 40,45, and then biennially after 50 has been recommended. This strategy has been shown to be more cost-effective compared with annual testing after age 50.<sup>2,39</sup>

### **Prostate-specific antigen density and velocity, and free prostate-specific antigen**

Over 80% of men with an elevated PSA will have a level between 4.0 and 10.0 ng/ml due to the high prevalence of BPH in the population.<sup>7</sup> Adjustment of PSA level by determination of prostate size via ultrasound has been proposed

**Table 40.1** *PSA thresholds based on age and race*

| Age (years) | 'Normal' PSA ranges (ng/ml)           |                          |                                       |                          |
|-------------|---------------------------------------|--------------------------|---------------------------------------|--------------------------|
|             | Based on 95% specificity <sup>a</sup> |                          | Based on 95% sensitivity <sup>b</sup> |                          |
|             | White males <sup>c</sup>              | Black males <sup>d</sup> | White males <sup>d</sup>              | Black males <sup>d</sup> |
| 40          | 0–2.5                                 | 0–2.4                    | 0–2.5                                 | 0–2.0                    |
| 50          | 0–3.5                                 | 0–6.5                    | 0–3.5                                 | 0–4.0                    |
| 60          | 0–4.5                                 | 0–11.3                   | 0–3.5                                 | 0–4.5                    |
| 70          | 0–6.5                                 | 0–12.5                   | 0–3.5                                 | 0–5.5                    |

<sup>a</sup>Upper limit of normal prostate-specific antigen (PSA) determined from 95th percentile of PSA among men without prostate cancer.

<sup>b</sup>Upper limit of normal PSA required to maintain 95% sensitivity for cancer detection.

<sup>c</sup>From Oesterling et al 1993.<sup>36</sup>

<sup>d</sup>From Morgan et al 1996.<sup>37</sup>

Source: reprinted with permission from Carter and Partin.<sup>2</sup>

as a means of identifying patients with elevated PSA levels resulting from BPH vs prostate cancer.<sup>40,41</sup> The quotient of PSA and ultrasound measured prostate volume is termed PSA density (PSAD). A PSAD of  $\geq 0.15$  has been proposed as a threshold for recommending prostate biopsy in patients with PSA levels between 4.0 and 10.0 ng/ml and no evidence of prostate cancer on DRE or TRUS.<sup>42,43</sup> However, the utility of PSAD for detection of prostate cancer is limited, since up to 50% of cancers found in men following the above guidelines would have been missed.<sup>7</sup> Furthermore, PSAD has not been shown to increase the ability to predict cancer in men with a normal DRE and PSA level between 4.0 and 10.0 ng/ml compared to using PSA alone.<sup>44</sup>

A change in the level of serum PSA over a period of time is known as PSA velocity.<sup>45</sup> It has been shown that a rate of change in PSA  $\geq 0.75$  ng/ml per year is a specific marker for the presence of prostate cancer.<sup>45</sup> PSA velocity is highly valuable in detecting prostate cancer and distinguishing it from BPH early in the course of the disease. Several studies have demonstrated that men with prostate cancer have a more rapid rise in PSA compared to men without prostate cancer up to 10 years before diagnosis.<sup>46–48</sup> The minimum length of time over which PSA velocity can be determined is 18 months, and three repeated PSA measurements have been shown to optimize the accuracy of PSA velocity for detection of cancer.<sup>46,47,49,50</sup> Parameters such as PSAD, PSA velocity, or age- and race-specific PSA ranges have been partially successful in enhancing the specificity of PSA.<sup>51</sup>

The majority of PSA in circulation is bound to either ACT or MG; however, in men with prostate cancer there is a higher proportion of serum PSA complexed to ACT compared to men without malignancy.<sup>52–55</sup> This results in a lower percentage of free PSA found in the serum of men with prostate cancer. Initial studies suggested that a threshold level of free/total PSA of 0.18 has been shown to significantly improve the ability to distinguish between patients with and without cancer compared to the use of total PSA alone.<sup>53</sup> It has also been suggested that PSA should be approximately 10% (no higher than 15%) of the total prostate weight (PSAD of 0.1–0.15) in benign disease.<sup>38</sup> The threshold value for free PSA that is optimal for both sensitivity and specificity of prostate cancer detection is dependent upon prostate size, since overlap in the percentage of free PSA is greatest in men with and without cancer who have enlarged prostates.<sup>56,57</sup> A free PSA threshold value of 25% has been shown to detect up to 95% of prostate cancer in

both Caucasian and AfricanAmerican men.<sup>58</sup> This finding indicates that race may not be a significant factor when using free PSA for detection of cancer. The utility of percent free PSA for distinguishing those men with and without prostate cancer is highest when total PSA levels are between 4.0 and 10.0 ng/ml.<sup>59</sup> Recent results also support a similar role of percent free PSA for detecting prostate cancer at lower PSA levels between 2.6 and 4.0 ng/ml.<sup>60</sup>

*Other serum markers: complexed PSA, pPSA, BPSA, hK-2, and PAP*

Measurement of PSA bound to other proteins such as ACT (complexed PSA) has also been used to identify men with prostate cancer.<sup>61</sup> Assays that measure complexed PSA have recently been approved by the Food and Drug Administration (FDA) for prostate cancer detection.<sup>62–65</sup> However, there are controversies about the replacement of percent free PSA by complexed PSA.<sup>66</sup> An alternative molecular form of free PSA known as BPSA has been isolated from the nodular BPH tissue in the transition zone of the prostate.<sup>67</sup> Purified BPSA contains two distinct cleavages at lysine 145 and lysine 182, and it is increased in the prostatic transition zone. The utility of this test for prostate cancer screening and detection is at present limited, however, because BPSA may in fact serve as a better marker for the severity of BPH than cancer. A proportion of uncomplexed PSA is found in circulation as the inactive zymogen precursor pro PSA (pPSA).<sup>68</sup> Elevated levels of pPSA are more highly correlated with prostate cancer than with BPH.<sup>69</sup> Serum pPSA may represent a more cancer-specific form of PSA; however, further studies are warranted to determine if pPSA is clinically useful for distinguishing prostate cancer from BPH.<sup>69,70</sup>

Human glandular kallikrein (hK2) is a serine protease that has approximately 78% amino acid sequence homology to PSA.<sup>71</sup> The activity of PSA may in part be regulated by hK2, since hK2 has been shown to cleave the precursor form of PSA.<sup>72,73</sup> The hK2 protein is found almost exclusively in the prostate and is up-regulated in poorly differentiated prostate cancer cells compared to normal tissues.<sup>74–76</sup> Although the ratio of hK2 to free PSA may increase the sensitivity of PSA to identify men with prostate cancer, the use of hK2 as a serum marker remains limited.<sup>77–79</sup>

Prostatic acid phosphatase (PAP) was the most widely used serum marker for prostate cancer prior to the availability of PSA.<sup>80</sup> Enzymatic phosphatase activity is not restricted to the prostate, and the use of PAP for monitoring prostate cancer has been largely supplanted by PSA, since PAP levels are often detectable even after complete removal of prostate tissue.<sup>2</sup> Preoperative PAP levels have been shown to be predictive of patient outcome after radical prostatectomy; however, the lower sensitivity and specificity of PAP in detection of prostate cancer compared to PSA has led to its significantly decreased use in clinical practice.<sup>81</sup> Serum PAP levels may provide important confirmatory information in patients in whom advanced disease is suspected.<sup>82</sup>

### **Histologic grading of prostate cancer**

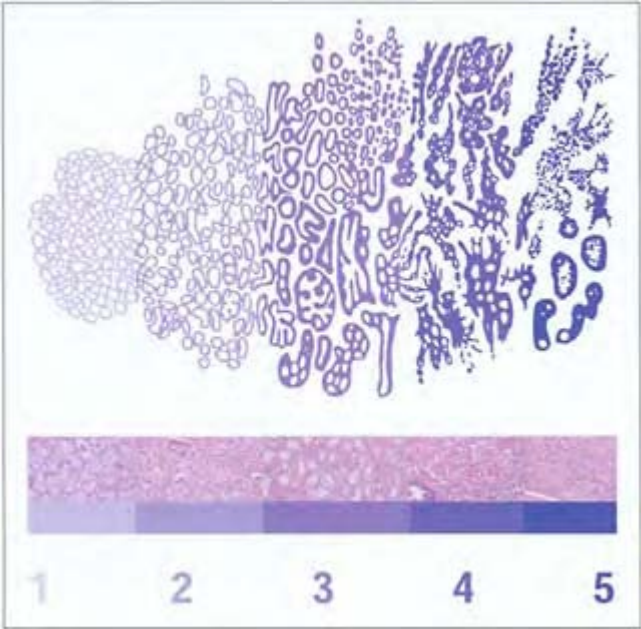
The Gleason histologic score is the most commonly used grading system for prostate cancer.<sup>83,84</sup> The Gleason system is based on microscopic analysis of tissue architecture

(Figure 40.1).<sup>85</sup> A Gleason pattern of 1–5 is assigned as a primary grade (most common pattern) and a secondary grade (second most common pattern). A Gleason sum of 2–10 is then obtained by addition of the primary grade to the secondary grade. The presence of a primary or secondary Gleason grade  $\geq 4$  or Gleason sum  $\geq 7$  has been associated with poorer prognosis.<sup>86–89</sup> Table 40.2 shows the distribution of Gleason grades found on prostate biopsy according to final pathologic stage in 2096 men who underwent surgery for clinically localized prostate cancer (Johns Hopkins series of 1982–1999).<sup>2</sup> Higher biopsy grade is associated with worse pathologic stage; however, on an individual basis, grade information alone does not accurately predict pathologic stage.

### Prostate cancer staging systems

Whitmore developed the initial clinical staging system for prostate cancer in 1956 which was subsequently modified by Jewett. The tumor, node, metastases (TNM) staging system adopted by the American Joint Committee for Cancer (AJCC) is currently the most widely used staging system.<sup>90,91</sup> The TNM system has undergone numerous revisions over the past several years, with the most recent update occurring in 2002 (Table 40.3). The most significant change in the 2002 TNM clinical staging system was stratification of palpable (T2) lesions into three different groups as follows: T2a, palpable tumor confined to less than one-half of one lobe; T2b, palpable tumor involving more than half of one lobe but not both lobes; and T2c, tumor involving both lobes (Figure 40.2). This modification was readopted, because the recurrence-free survival following treatment was significantly different using this system compared to the 1997 guidelines that combined clinical stages T2a and T2b.<sup>92,93</sup> The Gleason scoring system has also been emphasized as the grading system of choice and use of the terms well differentiated, moderately differentiated, and poorly differentiated is no longer recommended.<sup>94</sup>

Assessment of the extent of disease based on DRE, serum tumor markers, tumor grade, and imaging studies is termed clinical staging. Pathologic staging is more accurate in predicting disease involvement, since it is based upon histologic examination of the prostate specimen and lymph nodes after surgical removal. Prostate tumor grade, status of surgical margins, presence of extracapsular disease, seminal vesicle invasion, and pelvic lymph node involvement are the most important pathologic findings that are predictive of prognosis after radical prostatectomy.<sup>2</sup> Poor outcomes and recurrence with metastatic disease are associated with seminal vesicle invasion or lymph node metastases.<sup>13,88,95,96</sup> Perineural invasion (PNI) found in radical prostatectomy specimens has limited prognostic utility; however, an increased risk of non-organ confined disease at prostatectomy is associated with the presence of PNI in pretreatment biopsy cores.<sup>97</sup> The finding of PNI on biopsy is also associated with increased PSA level, poor tumor differentiation, and higher pathologic stage.<sup>98</sup>



**Figure 40.1** The Gleason scoring system: prostatic adenocarcinoma histologic grades.<sup>84</sup> Integrated design, R Sean Fulton. (Courtesy of Pittsburgh Supercomputing Center.)

**Table 40.2** *Comparison of biopsy Gleason grade and pathologic stages in 2096 men who underwent radical prostatectomy (John Hopkins series 1982–1999)*

| Grade | Organ confined<br>No. (%) | Capsular penetration<br>No. (%) | Seminal vesical<br>status No. (%) | Lymph node status<br>No. (%) |
|-------|---------------------------|---------------------------------|-----------------------------------|------------------------------|
| 2–4   | 54 (68)                   | 26 (30)                         | 2(2)                              | 0(0)                         |
| 5     | 162 (54)                  | 133 (44)                        | 3(1)                              | 4(1)                         |
| 6     | 756 (59)                  | 434 (34)                        | 42 (3)                            | 45 (4)                       |
| 7     | 105 (29)                  | 181 (51)                        | 28(8)                             | 43 (12)                      |
| 8–10  | 31 (29)                   | 36 (33)                         | 11 (10)                           | 30 (28)                      |

Source: reprinted with permission, from Carter and Partin.<sup>2</sup>

## Diagnostic imaging modalities

### *Transrectal ultrasound*

TRUS has become the most commonly used imaging modality for the prostate; however, the utility of TRUS as a screening method for localization of early prostate cancer remains limited.” Most hypoechoic lesions are not malignant and 50% of nonpalpable tumors larger than 1 cm in greatest dimension are not visualized by ultrasound.<sup>30,100,101</sup> Although hypoechoic areas on TRUS are more than twice as likely to contain cancer compared to isoechoic areas, up to 50% of cancers can potentially be missed if only hypoechoic areas are biopsied.<sup>2,30,32</sup> TRUS-guided biopsy of the prostate (Figure 40.3) can be utilized to obtain histologic confirmation of cancer once an individual has been identified as being at risk for the disease.<sup>102</sup> Systematic needle biopsy with TRUS is recommended to ensure accurate sampling of prostatic tissue in men who have an increased likelihood of harboring cancer.<sup>2</sup> Routine

**Table 40.3** *Prostate cancer staging systems*

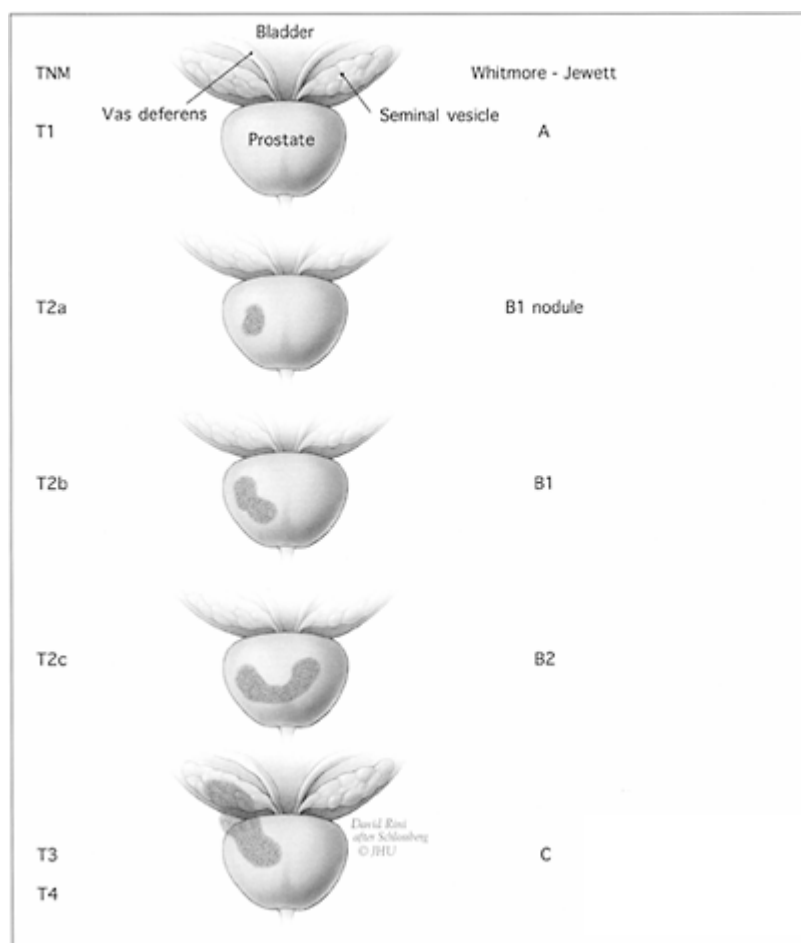
| TNM<br>2002 | Description  | Whitmore | Jewett Description  |
|-------------|--|----------|---|
| TX          | Primary tumor cannot be assessed   | None*    | None  |
| T0          | No evidence of primary tumor   | None     | None  |
| T1          | Nonpalpable tumor not evident by imaging   | A        | Same as TNM   |
| T1a         | Tumor found in tissue removed at TUR; 5% or less is cancerous and histological grade $\leq 7$  | A1       | Same as TNM   |
| T1b         | Tumor found in tissue removed at TUR; >5% is cancerous or histologic grade >7  | A2       | Same as TNM   |
| T1c         | Tumor identified by needle biopsy (e.g. because of elevated PSA)   | None     | None  |
| T2          | Palpable tumor confined to the prostate <sup>a</sup>   | B        | Same as TNM   |
| T2a         | Tumor involves less than one-half of one lobe  | B1N      | Tumor involves one-half lobe—surrounded by normal tissue on all sides |
| T2b         | Tumor involves more than one-half of a lobe but not both lobes   | B1       | Same as TNM   |
| T2c         | Tumor involves both lobes  | B2       | Same as TNM   |
| T3          | Tumor extends through the prostate capsule <sup>b</sup>  | C1       | Tumor <6 cm in diameter   |
| T3a         | Extracapsular extension (unilateral or bilateral)  | C1       | Same as TNM   |
| T3b         | Tumor invades seminal vesicle(s)   | C1       | Same as TNM   |
| T4          | Tumor is fixed or invades adjacent structures (not seminal vesicles): bladder neck, external sphincter, rectum, levator muscles, and/or pelvic wall. | C2       | Same as TNM   |
| None        | None   | DO       | Elevated prostatic acid phosphatase                                   |

|      |   |      |                             |
|------|---|------|-----------------------------|
| NX   | Regional lymph nodes cannot be assessed                         | None | None                        |
| N0   | No lymph node metastases  | None | None                        |
| N1   | Metastases in regional lymph node(s)                            | D1   | Same as TNM                 |
| MX   | Distant metastases cannot be assessed                           | None | None                        |
| M0   | No evidence of distant metastases                               | None | None                        |
| M1   | Distant metastases  | D2   | Same as TNM                 |
| M1a  | Involvement of nonregional lymph nodes                          | D2   | Same as TNM                 |
| M1b  | Involvement of bones  | D2   | Same as TNM                 |
| M1c  | Involvement of other distant sites with or without bone disease | D2   | Same as TNM                 |
| None | None  | D3   | Hormonal refractory disease |

<sup>a</sup> Tumor found in one or both lobes by needle biopsy, but not palpable or reliably visible by imaging is classified as T1c.

<sup>b</sup> Invasion into the prostatic apex or into (but not beyond) the prostatic capsule is classified not as T3 but as T2. TNM, tumor—node metastases staging system; TUR, transurethral resection; PSA, prostate-specific antigen.

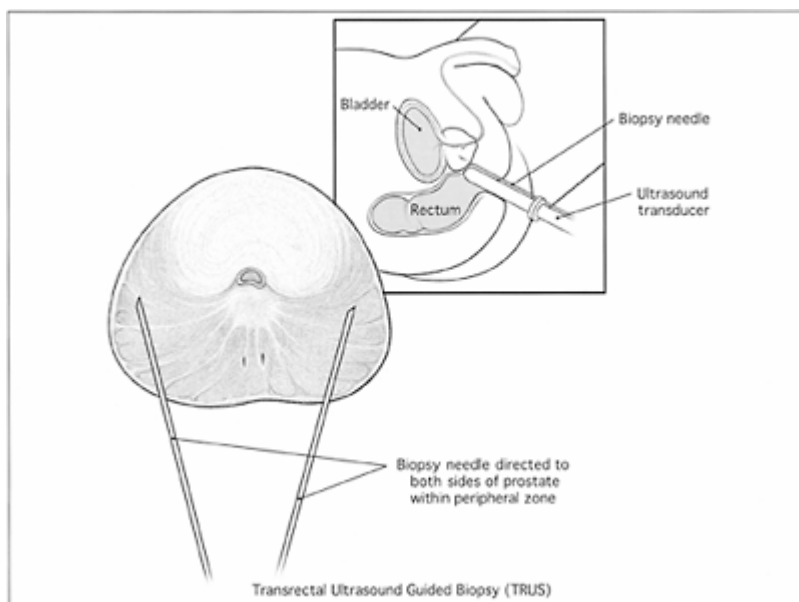
*Source:* adapted with permission from Carter and Partin.<sup>2</sup>



**Figure 40.2** Prostate cancer staging system. (Reprinted with permission from Walsh and Worthington.<sup>38</sup>)

sampling of sextant and posterolateral aspects of the gland with 12 cores sampled per patient is suggested. The combination of both sextant and posterolateral needle biopsies maximizes the detection of cancer, since up to 25% of prostate cancers may be missed if only routine sextant needle biopsy is performed.<sup>103</sup> Some patients, however, may not be candidates for TRUS-guided biopsy (e.g. previous history of bowel/rectal surgery or inflammatory disease process). An alternative, yet not commonly utilized, method for obtaining prostatic tissue for pathologic diagnosis of cancer is via the transperineal approach under ultrasound or magnetic resonance imaging (MRI) guidance.<sup>104,105</sup>





**Figure 40.3** Transrectal ultrasound (TRUS)-guided biopsy of the prostate. (Reprinted with permission from Walsh and Worthington.<sup>38</sup>

#### *Radionuclide bone scan*

The utility of radionuclide bone scan in patients with localized disease is rather limited. Bone scintigraphy is not recommended for preoperative prostate cancer staging in patients with PSA values  $<10$  unless symptomatic bone pain is present.<sup>106</sup> On the other hand, radionuclide bone scan has been shown to be the most sensitive method for detecting bone metastases.<sup>107,108</sup> Bone scans may provide more useful information for patients with advanced disease (PSA  $>10$ , Gleason score  $>7$ , clinical stage T3 or higher). An appropriate treatment algorithm including hormonal therapy can be initiated if bone metastases are detected. Positive findings on bone scan are not always specific for prostate cancer, since any inflammatory or wound healing processes (e.g. recent fracture, osteomyelitis) may be interpreted as a false-positive result. Radionuclide bone imaging has also been shown to be helpful in detecting urinary tract obstruction (including upper tracts) and assessing bilateral renal function.<sup>109</sup>

#### *Computed tomography, magnetic resonance imaging, magnetic resonance spectroscopic imaging, and ProstaScint™*

Abdominal and pelvic computed tomography (CT) scanning provides little useful diagnostic or staging information, especially in patients with PSA  $<20$  ng/ml.<sup>110–112</sup> use

of pelvic CT would not benefit the majority of patients whose prostate cancers were detected by DRE and PSA testing, and may be of some limited value only in patients with advanced disease.<sup>2</sup> Diagnosis of lymph node metastases by CT scan is based primarily on size with any node >1 cm in diameter (short axis) considered abnormal. The sensitivity of positive lymph node detection based on size criteria (>1 cm) is approximately 25–78% and specificity is approximately 90%.<sup>113,114</sup>

Endorectal coil MRI has limited value in staging localized disease at the present time. Pelvic phase-arrayed coil MRI has been shown to predict positive surgical margins with up to 75% accuracy in some studies.<sup>115,116</sup> The sensitivity and specificity of pelvic coil MRI for prediction of capsular penetration and seminal vesicle invasion has been reported to be approximately 50% and 92%, respectively. MRI for prostate cancer staging may be more useful in the detection of lymph node metastases in men who are at high risk. MRI may provide additional information in patients with PSA levels between 10 and 20 ng/ml, Gleason score  $\leq 7$ , and  $\geq 50\%$  positive biopsies on sextant sampling.<sup>106</sup>

Quantitative magnetic resonance spectroscopic imaging (MRSI) is a recent advance in MR technology that permits evaluation of cellular metabolism and anatomy of the prostate. MRSI can be utilized to define tumor volume through functional or metabolic imaging differences compared to normal prostate tissue. Detection of extraprostatic disease can be significantly improved by combining MRI findings with estimates of metabolic abnormalities provided by MRSI.<sup>117</sup> MRSI has been shown to be significantly better than TRUS and MRI in differentiating among prostate cancer, BPH, and necrosis in patients suspected of having recurrent disease after cryosurgery.<sup>118</sup> The addition of MRSI to MRI has also been reported to increase the overall accuracy of prostate cancer tumor volume measurement; however, MRSI is not routinely used for pretreatment prostate cancer staging at the present time.

Capromab pendetide scanning (ProstaScint™) utilizes an Indium<sup>111</sup>-radiolabeled antibody (capromab pendetide or CYT-356) directed against prostate-specific membrane antigen (PSMA) for detection of cancer. This test may be most useful when other diagnostic studies have failed to identify metastatic disease in high-risk patients or in patients with evidence of biochemical recurrence after radical prostatectomy. ProstaScint has been approved by the FDA for evaluation of newly diagnosed patients at high risk for metastases. Patients who are appropriate candidates for ProstaScint typically have a Gleason score  $\geq 7$  and PSA >20 ng/ml; Gleason score of 8–10 regardless of PSA value; or Gleason score  $\geq 6$  and clinical stage T3 disease.<sup>106</sup>

### Prediction of pathologic stage

The accuracy of prostate cancer staging is significantly enhanced by considering the following parameters: extent of local disease (T stage), serum PSA level, and Gleason grade obtained from biopsy.<sup>18,119–122</sup> An increasing number of men over the past decade have presented with nonpalpable (stage T1c) disease, PSA levels <10 ng/ml, and well to moderately differentiated tumors (Gleason score 4–6). This downward stage migration which may be attributed to the utility of PSA and better screening strategies has resulted in approximately 60% of newly diagnosed cases presenting with localized or regional disease.<sup>1</sup> Staging nomograms (Table 40.4) have been constructed and further validated

based on clinical stage, serum PSA level, and Gleason grade from the biopsy specimen.<sup>123</sup> The nomograms are also referred to as the Partin tables and values represent the percent probability of having the indicated final pathologic stage based on logistic regression analyses for all three variables combined.

The Partin tables were designed in order to provide patients with information that could be used for treatment decision making based on prediction of pathologic stage before definitive therapy. The likelihood of having organconfined disease, capsular penetration, cancer in the seminal vesicles, and cancer in the lymph nodes is predicted with 95% accuracy. The 2001 Partin tables reflect the improvement in cancer control that has occurred with earlier diagnosis of disease and stage migration.<sup>122</sup> Important factors that must be considered in disease management include age, race, and the presence of low-volume (stage T1c) disease.<sup>38</sup> Older men tend to have larger-volume tumors and more aggressive disease (Gleason score  $\geq 7$ ).<sup>124</sup> Ethnic background is important, since African-American men are more likely to develop prostate cancer and are also more likely to die from the disease than other ethnic groups.<sup>38</sup> Approximately 25% of men diagnosed with nonpalpable (T1c) disease will have low-volume disease ( $<0.2 \text{ cm}^3$ ).<sup>125</sup> Consideration of factors such as specific findings on needle biopsy, PSA density, and percentage of free PSA may be useful in determining whether stage T1c cancer is significant (Table 40.5).<sup>38</sup>

### Clinical staging procedures

Clinical staging procedures such as laparoscopic or minilaparotomy (mini-lap) pelvic lymphadenectomy should be reserved for situations in which it is unclear whether a patient has localized disease. Appropriate candidates for such staging procedures would have clinically localized prostate cancer and have high risk for extraprostatic lymph node involvement. These staging procedures should not be performed on men with clear evidence of advanced disease (i.e. positive bone scan). The probability of disease recurrence after radical prostatectomy in a patient with Gleason score 8 disease and positive lymph nodes is approximately 85% within 5 years.<sup>38</sup> Histologic examination of lymph nodes may be less important in men with Gleason score  $\leq 7$  cancers, because positive lymph nodes in this group are unlikely and associated with a  $<15\%$  probability of metastatic disease at 5 years.<sup>38</sup> Therefore, staging pelvic lymphadenectomy is recommended for men with

**Table 40.4** *Prostate cancer staging nomograms  
(2001 Partin tables)*



| PSA range<br>(ng/ml)                           | Pathologic stage         | Gleason score |            |            |            |            |
|--|--------------------------|---------------|------------|------------|------------|------------|
|  |                          | 2–4           | 5–6        | 3+4=7      | 4+3=7      | 8–10       |
| Clinical stage T1c (nonpalpable, PSA elevated) |                          |               |            |            |            |            |
| 0–2.5  | Organ confined           | 95 (89–99)    | 90 (88–93) | 79 (74–85) | 71 (62–79) | 66 (54–76) |
|  | Extraprostatic extension | 5 (1–11)      | 9 (7–12)   | 17 (13–23) | 25 (18–34) | 28 (20–38) |
|  | Seminal vesicle ( + )    | –             | 0 (0–1)    | 2 (1–5)    | 2 (1–5)    | 4(1–10)    |

|  |                          |               |            |            |            |            |
|--|--------------------------|---------------|------------|------------|------------|------------|
| 2.6–4.0                                    | Lymph node ( + )         | –             |            | 1 (0–2)    | 1(0–4)     | 1(0–4)     |
|  | Organ confined           | 92 (82–98)    | 84 (81–86) | 68 (62–74) | 58 (48–67) | 52 (41–63) |
|  | Extraprostatic extension | 8 (2–18)      | 15 (13–18) | 27 (22–33) | 37 (29–46) | 40 (31–50) |
| 4.1–6.0                                    | Seminal vesicle (+)      | –             | 1 (0–1)    | 4 (2–7)    | 4 (1–7)    | 6 (3–12)   |
|  | Lymph node (+)           | –             |            | 1 (0–2)    | 1 (0–3)    | 1(0–4)     |
|  | Organ confined           | 90 (78–98)    | 80 (78–83) | 63 (58–68) | 52 (43–60) | 46 (36–56) |
| 6.1–10.0                                   | Extraprostatic extension | 10 (2–22)     | 19 (16–21) | 32 (26–36) | 42 (35–50) | 45 (36–54) |
|  | Seminal vesicle (+)      | –             | 1 (0–1)    | 3 (2–5)    | 3 (1–6)    | 5 (3–9)    |
|  | Lymph node (+)           | –             | 0 (0–1)    | 2 (1–3)    | 3 (1–5)    | 3 (1–6)    |
| > 10.0                                     | Organ confined           | 87 (73–97)    | 75 (72–77) | 54 (49–50) | 43 (35–51) | 37 (28–46) |
|  | Extraprostatic extension | 13 (3–27)     | 23 (21–25) | 36 (32–40) | 47 (40–54) | 48 (39–57) |
|  | Seminal vesicle (+)      | –             | 2 (2–3)    | 8(6–11)    | 8 (4–12)   | 13 (8–19)  |
| Clinical stage T2a (palpable <of one lobe) | Lymph node (+)           | –             | 0 (0–1)    | 2 (1–3)    | 2 (1–4)    | 3 (1–5)    |
|  | Organ confined           | 80 (61–95)    | 62 (58–64) | 37 (32–53) | 27 (21–34) | 22 (16–30) |
|  | Extraprostatic extension | 20 (5–39)     | 33 (30–36) | 43 (38–48) | 51 (44–59) | 50 (42–59) |
| 0–2.5                                      | Seminal vesicle ( + )    | –             | 4 (3–5)    | 12 (9–17)  | 11 (6–17)  | 17 (10–25) |
|  | Lymph node (+)           | –             | 2 (1–3)    | 8 (5–11)   | 10 (5–17)  | 11 (5–18)  |
|  | Organ confined           | 91 (79–98)    | 81 (77–85) | 64 (56–71) | 53 (43–63) | 47 (35–59) |
| 2.6–4.0                                    | Extraprostatic extension | 9 (2–21)      | 17 (13–21) | 29 (23–36) | 40 (30–49) | 42 (32–53) |
|  | Seminal vesicle (+)      | –             | 1(0–2)     | 5 (1–9)    | 4(1–9)     | 7 (2–16)   |
|  | Lymph node (+)           | –             | 0 (0–1)    | 2 (0–5)    | 3 (0–8)    | 3 (0–9)    |
| 2.6–4.0                                    | Organ confined           | 85 (69–96)    | 71 (66–75) | 50 (43–57) | 39 (30–48) | 33 (24–44) |
|  | Extraprostatic extension | 15 (4–31)     | 27 (23–31) | 41 (35–58) | 52 (43–61) | 53 (44–63) |
|  | Seminal vesicle (+)      | –             | 2 (1–3)    | 7 (3–12)   | 6 (2–12)   | 10 (4–18)  |
| PSA range (ng/ml)                          | Lymph node (+)           | –             | 0 (0–1)    | 2(0–4)     | 2 (0–6)    | 3 (0–8)    |
|  | Pathologic stage         | Gleason score |            |            |            |            |
|  |                          | 2–4           | 5–6        | 3+4=7      | 4+3=7      | 8–10       |



Clinical stage T2a (palpable of one lobe)

|         |                |            |            |            |            |            |
|---------|----------------|------------|------------|------------|------------|------------|
| 4.1–6.0 | Organ confined | 81 (63–95) | 66 (62–70) | 44 (39–50) | 33 (25–41) | 28 (20–37) |
|---------|----------------|------------|------------|------------|------------|------------|

|  |                          |            |            |            |            |            |
|--|--------------------------|------------|------------|------------|------------|------------|
| 6.1–10.0   | Extraprostatic extension | 19 (5–37)  | 32 (28–36) | 46 (40–52) | 56 (48–64) | 58 (49–66) |
|  | Seminal vesicle (+)      | –          | 1 (1–2)    | 5 (3–8)    | 5 (2–8)    | 8 (4–13)   |
|  | Lymph node (+)           | –          | 1 (0–2)    | 4 (2–7)    | 6 (3–11)   | 6 (2–12)   |
|  | Organ confined           | 76 (56–94) | 58 (54–61) | 35 (30–40) | 25 (19–32) | 21 (15–28) |
|  | Extraprostatic extension | 24 (6–44)  | 37 (34–41) | 49 (43–54) | 58 (51–66) | 57 (48–65) |
| >10.0  | Seminal vesicle (+)      | –          | 4 (3–5)    | 13 (9–18)  | 11 (6–17)  | 17 (11–26) |
|  | Lymph node (+)           | –          | 1 (0–2)    | 3 (2–6)    | 5 (2–8)    | 5 (2–10)   |
|  | Organ confined           | 65 (43–89) | 42 (38–46) | 20 (17–24) | 14 (10–18) | 11 (7–15)  |
|  | Extraprostatic extension | 35 (11–57) | 47 (43–52) | 49 (43–55) | 55 (46–64) | 52 (41–62) |
|  | Seminal vesicle (+)      | –          | 6 (4–8)    | 16 (11–22) | 13 (7–20)  | 19 (12–29) |
|  | Lymph node (+)           | –          | 4 (3–7)    | 14 (9–21)  | 18 (10–27) | 17 (9–29)  |
|   |                          |            |            |            |            |            |
| Clinical stage T2b (palpable  of one lobe, not on both lobes) |                          |            |            |            |            |            |
| 0–2.5  | Organ confined           | 88 (73–97) | 75 (69–81) | 54 (46–63) | 43 (33–54) | 37 (26–49) |
|  | Extraprostatic extension | 12 (3–27)  | 22 (17–28) | 35 (28–43) | 45 (35–56) | 46 (35–58) |
|  | Seminal vesicle (+)      | –          | 2 (0–3)    | 6 (2–12)   | 5 (1–11)   | 9 (2–20)   |
|  | Lymph node (+)           | –          | 1 (0–2)    | 4 (0–10)   | 6 (0–14)   | 6 (0–16)   |
|  | Organ confined           | 80 (61–95) | 63 (57–69) | 41 (33–48) | 30 (22–39) | 25 (17–34) |
| 2.6–4.0  | Extraprostatic extension | 20 (5–39)  | 34 (28–40) | 47 (40–55) | 57 (47–67) | 57 (46–68) |
|  | Seminal vesicle (+)      | –          | 2 (1–4)    | 9 (4–15)   | 7 (3–14)   | 12 (5–22)  |
|  | Lymph node (+)           | –          | 1 (0–2)    | 3 (0–8)    | 4 (0–12)   | 5 (0–14)   |
|  | Organ confined           | 75 (55–93) | 57 (52–63) | 35 (29–40) | 25 (18–32) | 21 (14–29) |
|  | Extraprostatic extension | 25 (7–45)  | 39 (33–44) | 51 (44–57) | 60 (50–68) | 59 (49–69) |
| 4.1–6.0  | Seminal vesicle (+)      | –          | 2 (1–3)    | 7 (4–11)   | 5 (3–9)    | 9 (4–16)   |
|  | Lymph node (+)           | –          | 2 (1–3)    | 7 (4–13)   | 10 (5–18)  | 10 (4–20)  |
|  | Organ confined           | 69 (47–91) | 49 (43–54) | 26 (22–31) | 19 (14–25) | 15 (10–21) |
|  | Extraprostatic extension | 31 (9–53)  | 44 (39–49) | 52 (46–58) | 60 (52–68) | 57 (48–67) |
|  | Seminal vesicle (+)      | –          | 5 (3–8)    | 16 (10–22) | 13 (7–20)  | 19 (11–29) |
| 6.1–10.0   | Lymph node (+)           | –          | 2 (1–3)    | 6 (4–10)   | 8 (5–14)   | 8 (4–16)   |
|  | Organ confined           | 57 (35–86) | 33 (28–38) | 14 (11–17) | 9 (6–13)   | 7 (4–10)   |
|  | Extraprostatic extension | 31 (9–53)  | 44 (39–49) | 52 (46–58) | 60 (52–68) | 57 (48–67) |
|  | Seminal vesicle (+)      | –          | 5 (3–8)    | 16 (10–22) | 13 (7–20)  | 19 (11–29) |
|  | Lymph node (+)           | –          | 2 (1–3)    | 6 (4–10)   | 8 (5–14)   | 8 (4–16)   |
| >10.0  | Organ confined           | 57 (35–86) | 33 (28–38) | 14 (11–17) | 9 (6–13)   | 7 (4–10)   |
|  | Extraprostatic extension | 31 (9–53)  | 44 (39–49) | 52 (46–58) | 60 (52–68) | 57 (48–67) |
|  | Seminal vesicle (+)      | –          | 5 (3–8)    | 16 (10–22) | 13 (7–20)  | 19 (11–29) |
|  | Lymph node (+)           | –          | 2 (1–3)    | 6 (4–10)   | 8 (5–14)   | 8 (4–16)   |
|  | Organ confined           | 57 (35–86) | 33 (28–38) | 14 (11–17) | 9 (6–13)   | 7 (4–10)   |

|   | Extraprostatic extension | 43 (14–65)    | 52 (46–56) | 47 (40–53) | 50 (40–60) | 46 (36–59) |
|---|--------------------------|---------------|------------|------------|------------|------------|
|   | Seminal vesicle (+)      | –             | 8 (5–11)   | 17 (12–24) | 13 (8–21)  | 19 (12–29) |
|   | Lymph node (+)           | –             | 8 (5–12)   | 22 (15–30) | 27 (16–39) | 27 (14–40) |
| PSA range (ng/ml)                           | Pathologic stage         | Gleason score |            |            |            |            |
|   |                          | 2–4           | 5–6        | 3+4=7      | 4+3=7      | 8–10       |
| Clinical stage T2c (palpable on both lobes) |                          |               |            |            |            |            |
| 0–2.5                                       | Organ confined           | 86 (17–97)    | 73 (63–81) | 51 (38–63) | 39 (26–54) | 34 (21–48) |
|   | Extraprostatic extension | 14 (3–29)     | 24 (17–33) | 36 (26–48) | 45 (32–59) | 47 (33–61) |
|   | Seminal vesicle ( + )    | –             | 1 (0–4)    | 5 (1–13)   | 5 (1–12)   | 8 (2–19)   |
|   | Lymph node ( + )         | –             | 1 (0–4)    | 6 (0–18)   | 9 (0–26)   | 10 (0–27)  |
| 2.6–4.0                                     | Organ confined           | 78 (58–94)    | 61 (50–70) | 38 (27–50) | 27 (18–40) | 23 (14–34) |
|   | Extraprostatic extension | 22 (6–42)     | 36 (27–45) | 48 (37–59) | 57 (44–70) | 57 (44–70) |
|   | Seminal vesicle ( + )    | –             | 2 (1–5)    | 8 (2–17)   | 6 (2–16)   | 10 (3–22)  |
|   | Lymph node ( + )         | –             | 1(0–4)     | 5 (0–15)   | 7 (0–21)   | 8 (0–22)   |
| 4.1–6.0                                     | Organ confined           | 73 (52–93)    | 55 (44–64) | 31 (23–41) | 21 (41–31) | 18(11–28)  |
|   | Extraprostatic extension | 27 (7–48)     | 49 (32–50) | 50 (40–60) | 57 (43–68) | 57 (43–70) |
|   | Seminal vesicle ( + )    | –             | 2(1–4)     | 6(2–11)    | 4(1–10)    | 7 (2–15)   |
|   | Lymph node (+)           | –             | 3 (1–7)    | 12 (5–23)  | 16 (6–32)  | 16 (6–33)  |
| 6.1–10.0                                    | Organ confined           | 67 (45–91)    | 46 (36–56) | 24 (17–32) | 16(10–24)  | 13 (8–20)  |
|   | Extraprostatic extension | 33 (9–55)     | 46 (37–55) | 52 (42–61) | 58 (46–69) | 56 (43–69) |
|   | Seminal vesicle ( + )    |               | 5 (2–9)    | 13 (6–23)  | 11 (4–21)  | 16 (6–29)  |
|   | Lymph node (+)           |               | 3 (1–6)    | 10 (5–18)  | 13 (6–25)  | 13 (5–26)  |
| >10.0                                       | Organ confined           | 54 (32–85)    | 30 (21–38) | 11 (7–17)  | 7 (4–12)   | 6 (3–10)   |
|   | Extraprostatic extension | 46 (15–68)    | 51 (42–60) | 42 (30–55) | 43 (29–50) | 41 (27–57) |
|   | Seminal vesicle (+)      |               | 6 (2–12)   | 13 (6–24)  | 10 (3–20)  | 15 (5–28)  |
|   | Lymph node (+)           |               | 13 (6–22)  | 33 (18–49) | 38 (20–58) | 38 (20–59) |

PSA=prostate-specific antigen.

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**Table 40.5** *Determination of significant vs insignificant stage T1c (nonpalpable) disease.*<sup>38</sup>

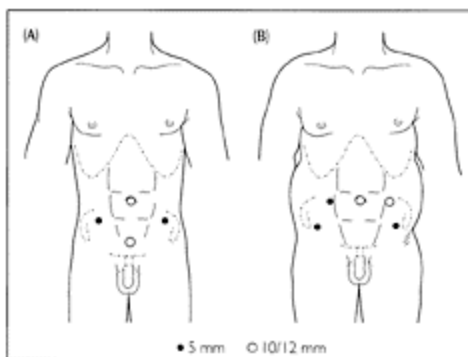
| Significant T1c cancer  | Insignificant T1c cancer                           |
|---|--|
| Cancer identified in 3 needle cores, or   | Cancer identified in only 1 or 2 needle cores, and |
| Cancer present in greater than half of any one core, or   | Cancer present in less than half of each core, and |
| Gleason score $\geq 7$ , or   | Gleason score $\leq 6$ , and                       |
| PSA density $>0.1\text{--}0.15$ , or  | PSA density $<0.1\text{--}0.15$ , and              |
| Free PSA $<15\%$  | Free PSA $>15\%$                                   |
| These factors apply only if cancer is nonpalpable and if biopsies have included at least six cores. |  |

PSA  $\geq 15$  ng/ml, Gleason score  $\geq 8$  disease, or TNM stage T2b or greater who are candidates for surgery, and who are potentially curable.

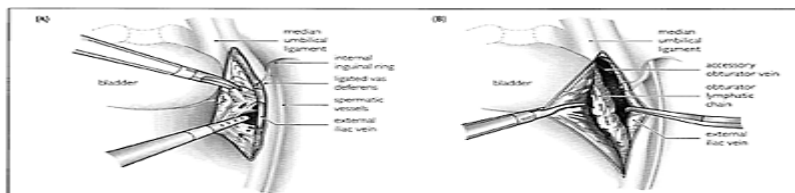
#### *Operative technique for limited laparoscopic pelvic lymphadenectomy*

The use of laparoscopic pelvic lymphadenectomy for prostate cancer staging was first introduced in 1991.<sup>126</sup> Transperitoneal laparoscopic pelvic lymphadenectomy may be accomplished using either the diamond or fan configurations for trochar placement (Figure 40.4). The diamond configuration is formed by placement of trochars as follows: two 10 mm ports at the umbilicus and 4–6 cm superior to the pubic symphysis in the midline; two 5 mm ports located near McBurney's point in the midclavicular line bilaterally. The fan configuration may be utilized for obese patients or men with a dense urachus.<sup>127</sup> The fan configuration comprises 5 trochars placed in the following locations: a 10 mm umbilical trochar for the laparoscope; two trochars at the level of the umbilicus and lateral to the inferior epigastric vessels in line with the anterior superior iliac crest (a 10 mm trochar on the left side and a 5 mm trochar on the right side); and two 5 mm trochars placed laterally and midway between the umbilicus and pubic symphysis.

After insufflation of the abdomen and division of the vas deferens, the external iliac vein is identified to define the lateral extent of the dissection. Pulsations of the external iliac artery can serve as a helpful landmark in identifying the location of the external iliac vein (Figure 40.5). The fatty tissue inferior to the arterial pulsation is elevated and gently dissected in order to expose the



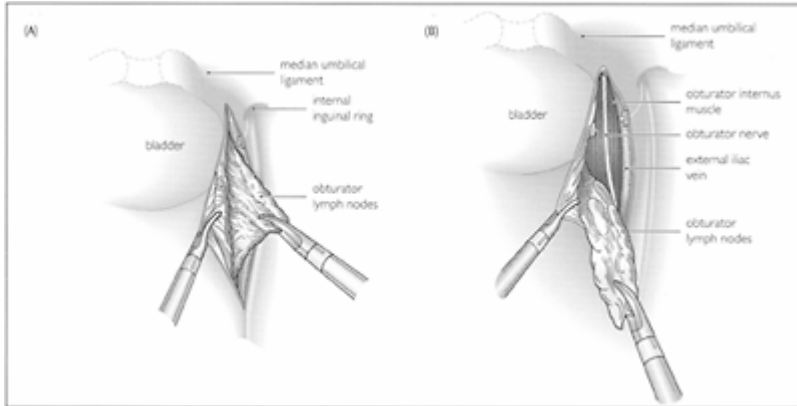
**Figure 40.4** Placement of trochars for laparoscopic pelvic lymphadenectomy. (A) Diamond configuration: two 10 mm trochars at umbilicus and 4–6 cm above the pubic symphysis in the midline; two 5 mm trochars near McBurney's point in the midclavicular line bilaterally. (B) Fan configuration: 10 mm umbilical trochar; 10 mm on left and 5 mm trochar on right at the level of the umbilicus, lateral to the inferior epigastric vessels in line with the anterior superior iliac crest; two 5 mm trochars are also placed laterally and midway between the umbilicus and pubic symphysis.



**Figure 40.5** Laparoscopic pelvic lymphadenectomy. (A) The pulsation of the external iliac artery is used to identify the external iliac vein. Blunt dissection with the irrigator-aspirator is



used to facilitate mobilization of the lymph node packet from the anterior surface of the vein. (B) The lymphatic tissue is mobilized free from the bifurcation of the common iliac vein to the pubis and medially until the obturator internus muscle is visualized.



**Figure 40.6** Laparoscopic pelvic lymphadenectomy . (A) The inferior portion of the lymph node packet is isolated and divided near the circumflex iliac artery in order to avoid injury to the obturator nerve. (B) The lymph node packet is gently freed from the obturator nerve and pelvic sidewall using blunt dissection. The remaining pedicle is clipped in addition to any open lymphatic channels and small blood vessels prior to removal of the lymph node packet.

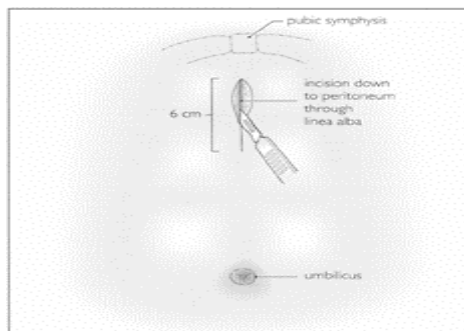
external iliac vein. The lymphatic tissue is then mobilized free from the bifurcation of the common iliac vein to the pubis and medially until the obturator internus muscle is visualized. The dissection proceeds along the lateral pelvic sidewall to the inferior portion of the iliac vein. Once this portion of the dissection is completed, the inferior aspect of the lymph node packet is divided near the circumflex iliac artery and femoral canal to avoid injury to the obturator nerve (Figure 40.6). Removal of the lymph node

packet is facilitated by blunt dissection and retraction in a cephalad direction. Sharp dissection should be avoided to minimize iatrogenic nerve and vascular injury. Hemoclips can be applied to any small lymphatic structures or vessels coursing between the pelvic sidewall and the lymph node packet. Following removal of the lymph node packet, hemostasis should be assessed under low insufflation pressures (i.e. 5–10 mmHg).

#### *Operative technique for minilaparotomy pelvic lymphadenectomy*

The mini-lap approach was first introduced in 1992 as an alternative to laparoscopic pelvic lymphadenectomy.<sup>128</sup> This technique has proven to be versatile in lymph node sampling in patients at risk for harboring metastatic disease. In the mini-lap approach, a 6 cm lower midline abdominal incision is made approximately 2 cm above the pubic symphysis (Figure 40.7). The anterior rectus fascia and transversalis fascia are sharply incised in the midline between the rectus muscles to enter the space of Retzius. The peritoneum is then mobilized off the external iliac vessels up to the bifurcation of the common iliac arteries. Removal of the lymph node packet is initiated by incision of the lymphatic tissue overlying the medial aspect of the external iliac vein (Figure 40.8). A metal clip is placed proximal to the node of Cloquet, followed by an incision proximal to the clip in order to remove the distal node packet. Care should be taken to avoid injury to the accessory obturator vein which may present and coursing from the obturator foramen to the external iliac vein. The lymph node packet is removed en bloc from the pelvic sidewall with preservation of the obturator nerve and vessels.

The mini-lap procedure has been reported to be more cost-effective and have less morbidity than the laparoscopic approach. In a community practice setting, operative time was shorter and complication rates were lower for patients undergoing mini-lap vs laparoscopic pelvic lymph node dissection.<sup>129</sup> A comparison of the modified open approach to laparoscopic and mini-lap procedures demonstrated equal staging efficacy with no difference in



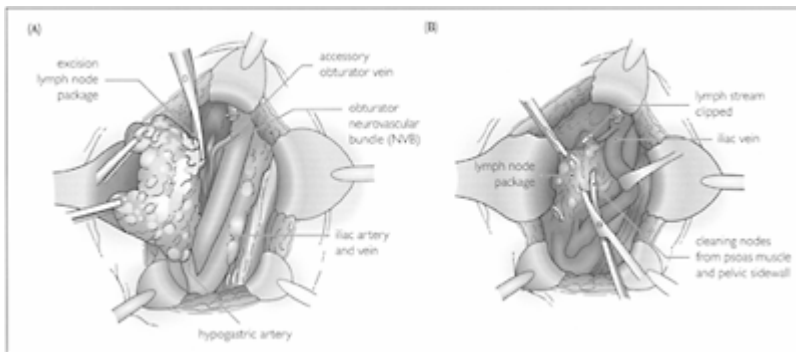
**Figure 40.7** Minilaparotomy (mini-lap) pelvic lymphadenectomy. A 6 cm lower midline abdominal incision is made approximately 2 cm above the

pubic symphysis. The anterior rectus fascia and transversalis fascia are sharply incised in the midline between the rectus muscles to enter the space of Retzius.

terms of the number of harvested lymph nodes.<sup>130</sup> The laparoscopic approach required significantly more operative time compared to the modified open and mini-lap techniques. Postoperative hospital recovery was similar for patients undergoing the mini-lap and laparoscopic pelvic lymph node dissection. The mini-lap approach has therefore been favored at institutions that are inexperienced with laparoscopic techniques.

### **Future directions: molecular markers for prostate cancer detection**

Most cancer detection assays are based on antibody interactions with marker proteins that are up-regulated in patients with prostate cancer. Advances in diagnostic techniques have resulted in the ability to detect circulating tumor cells in the blood of patients with prostate cancer. This may ultimately lead to diagnosis at earlier stages of disease when the primary lesion is potentially more curable. Molecular techniques such as polymerase chain reaction (PCR) and reverse transcriptase PCR (RT-PCR) are highly sensitive methods that have been utilized for detection of cancer cells. Over the past few years, numerous clinical studies have used PCR technology to detect genetic alterations, including mutations, deletions,



**Figure 40.8** Mini-lap pelvic lymphadenectomy. (A) Removal of the lymph node packet is initiated by incision of the lymphatic tissue overlying the medial aspect of the external iliac vein. A clip is placed

next to the external iliac vein and Cooper's ligament followed by incision of the lymph node packet boundary proximal to the clip. The distal lymph node packet is then mobilized. (B) The lymph node packet is removed en bloc from the obturator fossa.

translocations, and amplifications. RT-PCR is a sensitive method for detecting the presence of tumor-specific mRNA in cells isolated from peripheral blood. Several studies have characterized the presence of PSA-mRNA-bearing cells in the circulation of prostate cancer patients without evidence of metastatic disease.<sup>131</sup> A higher frequency of PS A-mRNA-expressing cells in the peripheral blood is correlated with extent of disease and has been shown to be an independent predictor of disease-free survival after radical prostatectomy.<sup>132</sup> The RT-PCR assay for PSA has been reported to be a better predictor of pathologic stage in men undergoing radical prostatectomy compared to PSA and Gleason score.<sup>133</sup>

PSMA is a 100 kDa type II transmembrane glycoprotein expressed in normal prostatic epithelium, BPH, prostatic intraepithelial neoplasia, and carcinoma.<sup>134,135</sup> Detectable PSMA levels have also been identified in duodenal mucosa and proximal renal tubules. The primary method for detection of PSMA expression has been with a monoclonal antibody that binds a six amino acid intracellular epitope of PSMA near the amino terminus.<sup>136</sup> Immunohistochemical staining of PSMA has been observed in vascular endothelium associated with tumors, which suggests a potential relationship between PSMA expression and angiogenesis.<sup>137</sup> Expression of PSMA may be dependent upon the degree of tumor differentiation, since lower levels have been observed in advanced prostate cancers.<sup>136</sup> The use of RT-PCR has been applied for detection of PSMA-expressing cells in blood with a reported sensitivity of 62–67%.<sup>138</sup> The potential clinical significance of detecting hematogenous micrometastatic disease remains promising; however, current RT-PCR strategies are not sensitive or accurate enough and in some cases may overpredict the extent of disease in early-stage cancer.

Prostate stem cell antigen (PSCA) is a homologue of the Thy-1/Ly-6 family of glycosylphosphatidylinositol (GPI)-anchored cell surface antigens and is expressed in the basal cells of normal prostate and in >80% of prostate cancers.<sup>139</sup> PSCA mRNA is up-regulated in both androgen dependent and independent prostate cancer xenografts. Increased PSCA expression measured by immunohistochemical analysis was observed in approximately 94% of primary prostate tumors and 100% of bone metastases.<sup>140</sup> PSCA expression was found to be increased with higher Gleason score, higher tumor stage, and progression to androgen independence. Although there have been no reports of PSCA detection in the circulation of patients with prostate cancer, further characterization of PSCA is needed to evaluate the prognostic utility of PSCA in prostate cancer.

The process of angiogenesis describes the dependence of solid tumors on development of new blood vessels required for growth, invasion, and metastasis.<sup>141</sup> Angiogenesis can be quantitated immunohistochemically by determination of microvessel density (MVD)

and may be of prognostic significance. The overall utility of angiogenesis as a prognostic tool for prostate cancer, however, remains controversial. Normal prostate tissue and prostate adenomas typically have low MVD, whereas the MVD in prostate cancer has been shown to increase significantly with tumor stage and grade.<sup>142</sup> MVD has also been shown to be an independent predictor of progression after radical prostatectomy in patients with Gleason score 5–7 disease.<sup>143</sup> In other studies, MVD was not associated with Gleason sum, tumor stage, surgical margin status, or seminal vesicle invasion.<sup>144,145</sup> Further investigation to assess the prognostic utility of angiogenesis markers is warranted, and may facilitate the development of antiangiogenic treatment strategies that target tumor vasculature.

DNA methylation is an epigenetic phenomenon that may also be used as a marker for prostate cancer. Methylation of gene promoter regions has been associated with transcriptional silencing. This process can affect many genes during tumorigenesis, including those involved in control of cellular growth.<sup>146</sup> Abnormal methylation of regulatory sequences at the glutathione S-transferase pi (GSTP1) gene locus is found in the majority (>90%) of prostate carcinomas but not in normal prostate tissue.<sup>147,148</sup> This methylation change has also been detected in urine and ejaculate specimens from patients with prostate cancer.<sup>149,150</sup> Aberrant methylation occurring in multiple genes has been shown to be correlated with poor clinical outcomes and may serve as a potentially useful tool for disease prognostication.<sup>151</sup> The clinical utility of methylation markers for prostate cancer detection or surveillance remains promising, but has not been validated at the present time.

Routine use of serum PSA and improvements leading to early detection have had a profound impact on the diagnosis and management of patients with prostate cancer. Current methods for preoperative assessment of disease prognosis are based on classic parameters such as clinical tumor stage, Gleason grade, and serum PSA level. Scientific advances over the past decade have led to the characterization of new molecular markers that may eventually prove to be more useful than PSA. An ideal marker is one with high sensitivity and specificity that could not only detect the presence or recurrence of prostate cancer but could also differentiate between an indolent tumor and an aggressive tumor with metastatic potential. Development of more sensitive and accurate measures of outcome is needed to improve upon existing treatments, and can only be achieved through a better understanding of the molecular basis of prostate cancer pathogenesis.

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## Perineal prostatectomy

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### Introduction

In the age of laparoscopy and other minimally invasive procedures, a discussion of the treatment of localized prostate cancer would be incomplete without the inclusion of radical perineal prostatectomy (RPP). The perineal prostatectomy is the oldest means of prostate resection and at one time was the standard of care for surgical treatment of localized prostate cancer. However, the procedure became less popular during the 1970s after studies published by Walsh and Donker demonstrated the advantages of a nerve-sparing technique using a retropubic approach.<sup>1</sup> The radical retropubic prostatectomy (RRP) became the urologist's preferred approach and the latest generation of surgeons was trained in this technique.

There has been a renewed interest in the perineal approach in recent years for a number of reasons. First, the research of Weldon and Tavel in the late 1980s applied Walsh's anatomic discoveries to the perineal approach, and opened the era of nerve-sparing RPP.<sup>2</sup> Secondly, concerns about the pelvic lymph nodes have been minimized as risk-assessment tables such as the Partin nomogram have clearly outlined which patients are at low risk for lymph node metastasis.<sup>3</sup> Couple this with the well-documented stage migration of prostate cancer and you have a large number of patients presenting with organ-confined disease and little chance of nodal involvement.

Since RPP has been practiced for decades, long-term data regarding the procedure are readily available.<sup>4,5</sup> Margin positivity, biochemical failure rates, and disease-specific mortality compare quite favorably with those reported in RRP series. Overall, early and late complications are equivalent between the two procedures, with the exception of an increased risk of rectal injury with RPP and a higher blood loss with RRP. Postoperative continence and potency rates are likewise quite similar.<sup>6,7</sup>

Perhaps the most compelling reason for the resurgence of the RPP is the introduction of laparoscopic prostatectomy. As the search for a minimally invasive, low-morbidity technique is evolving in the laparoscopic arena, other urologists are returning to RPP, a well-known, proven operation for the control of prostate cancer associated with very low estimated blood loss (EBL), shorter hospital stay, and quicker return to daily activities.

### Historical perspective

The perineal approach to the prostate dates back to the first century AD, when Celsus described a curvilinear incision anterior to the anus for removal of bladder stones.<sup>8</sup> In the modern era, credit is given to Bilroth for performing the first planned perineal prostatectomy in 1867.<sup>9</sup> In 1882, Leisrink modified the original technique of a median perineal incision by adding a curve over the region of the prostate. In addition, he described reconstruction of the urethra and the bladder neck.<sup>10</sup> All of these earlier advances culminated in the work of Hugh Hampton Young. Using a curvilinear approach, Young enucleated adenomatous tissue through the perineum to relieve bladder outlet obstruction. After finding evidence of carcinoma in several of these specimens, he undertook the task of perfecting a prostatectomy through the perineum with the intent of curing the disease. He performed autopsy studies and, with the assistance of Dr Halsted, performed the first radical perineal prostatectomy in 1904.<sup>11</sup> Young's technique is the foundation of the modern procedure and has undergone few modifications since its original description.

Vest described a modification of the closure of the wound, whereby the sutures passed through the vesicle neck and urethra and were subsequently tacked to the apex of the perineal wound to provide additional support for the anastomosis.<sup>12</sup> In a similar vein, Jewett described placement of a figure-of-eight suture along the posterior aspect of the vesicourethral anastomosis.<sup>13</sup> This suture began at the bladder neck, incorporated the urethra, and also gathered the urogenital diaphragm with the intent of providing extra support to the posterior aspect of the anastomosis.

Another significant contribution was introduced by Elmer Belt in 1939.<sup>14</sup> Belt described a new approach to perineal prostatectomy between the longitudinal fibers of the rectum and the circular fibers of the external anal sphincter. By approaching the surgery in this fashion, the prostate was exposed in a relatively bloodless field. However, he further modified Young's procedure in two key areas and was openly criticized by Young for these changes. First, he recommended leaving behind the apex of the prostate to achieve better urinary control. Secondly, he recommended opening the anterior layer of Denonvilliers' fascia during the dissection to expose the ampulla and seminal vesicles. Young considered these changes in violation of the principles of cancer surgery and recommended against their use in RPR.<sup>15</sup>

Perhaps the most relevant modification came after the sentinel work of Walsh and Donker with regard to RRP and the preservation of the cavernosal nerves and, thus, potency.<sup>1</sup> Modifying the principles described, Weldon and Tavel were able to successfully translate the nerve-sparing technique used in RRP to the perineal approach.<sup>2</sup> The modification entailed making a vertical incision in Denonvilliers' fascia as opposed to the classic transverse incision. This allowed reflection of the layer laterally over the apex of the gland and thus preservation of the neurovascular bundles.

## Patient selection

With renewed interest in the technique of perineal prostatectomy, the urologist must have a clear understanding of which patients are best suited for this technique. Prostatectomy is curative only if all of the cancer is removed; therefore, it should be reserved for those patients with organ-confined disease, a life expectancy longer than the natural history of the cancer (typically 10 years with prostate cancer), and no significant surgical risk factors. This includes patients with clinical stages T1b, T1c, or T2 tumors. A disqualifying age of approximately 75 years is reasonable given that a 75-year-old male has a survival of roughly 10.5 years.<sup>16</sup> Surgery should be delayed for 2 weeks following prostate biopsy and longer if the procedure was associated with any significant bleeding or infection.

## Anatomy

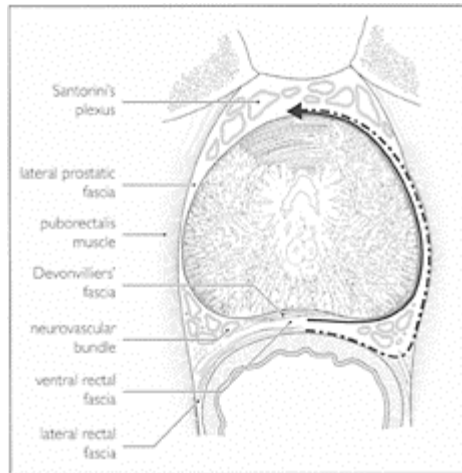
### *Pelvic fascia*

Surgeons preparing to undertake an RPP must have a clear understanding of the pelvic fascia, whether they intend to use the nerve-sparing technique or a wide dissection. The pelvic fascia is a single continuous layer that envelops all pelvic organs above the levator ani. Denonvilliers' fascia extends inferiorly from the peritoneal cul-de-sac, often to the level of the prostatic apex, while laterally it extends to envelop the neurovascular bundles. Typically, it is densely adherent to the posterior capsule of the prostate and becomes somewhat more tenuous overlying the seminal vesicles. It is separated from the rectum by the ventral rectal fascia, or the posterior lamella of Denonvilliers'.

### *Neurovascular bundles*

Knowledge of the course of the cavernous nerves is paramount when undertaking a nerve-sparing dissection. The nerves course caudally and ventrally as part of the neurovascular bundles. They lie within the lateral pelvic fascia and over the dorsolateral aspect of the prostate and membranous urethra (Figure 41.1). Most often these bundles are surrounded by a fatty layer that serves to make them readily identifiable visually. The nerves penetrate the urogenital diaphragm to reach their respective corpora.





**Figure 41.1** Transverse section through the perineum at the level of the verumontanum. The ventral rectal fascia is the key to the modern nerve-sparing dissection. The solid line represents the plane for a nerve-sparing approach on Denonvilliers' fascia and underneath the ventral rectal fascia. The dashed line lies outside all fascial planes and is followed for a wide, extended dissection.

### Advantages and disadvantages of the two techniques

Comparative data suggest that RPP and RRP offer equivalent cancer control rates for localized carcinoma of the prostate. Short- and long-term complication rates of the procedures are likewise very similar, with the exception of higher blood loss associated with RRP and an increased incidence of rectal injuries for RPP.<sup>7</sup> Further details are discussed at length later in the chapter.

RPP provides the distinct advantage of accessing the prostate at its most superficial location through a small perineal incision. Because of this, patients experience low morbidity, minimal postoperative pain, and thus have a short hospital stay. Published reports by Ruiz-Deya et al and Parra have documented discharge within 24 hours in 91% and 82% of patients, respectively.<sup>17,18</sup> The second major advantage is direct visualization and easy access to the apex and membranous urethra. This allows not only for improvement in dissection but also for direct visualization of the vesicourethral anastomosis. A third advantage is that the perineal resection is carried out underneath the

dorsal venous complex and thus results in significantly less blood loss. Anecdotally, the authors believe that salvage prostatectomy after radiation is often easier via the perineal approach, as it allows for a direct access to the prostate and sharp dissection of the rectum away from the overlying prostate gland.

Disadvantages likewise exist. Of concern historically was the inability to access the lymph nodes through the same incision. Recent studies, however, outline specific guidelines using prostate-specific antigen (PSA), clinical stage, and grade to determine which patients do not routinely need lymph node dissection. Pelvic lymph node dissection can safely be omitted in patients with PSA  $\leq 10$  ng/mL, Gleason sum  $\leq 6$ , and clinical stage T2b or less.<sup>19</sup> Another disadvantage is the exaggerated lithotomy position. While generally well tolerated, patients with conditions such as hip ankylosis, morbid obesity, and lower extremity amputations may not be candidates for this technique. A simple office test involves having the patient lie supine on the examination table and bringing his knees to his chest. If the patient is able to tolerate this test, he will probably be able to tolerate the position for RPP. However, after positioning in the operating room, ventilatory pressures  $>40$  cmH<sub>2</sub>O, or difficulties oxygenating the patient will infrequently result in the inability to perform RPP.

A third disadvantage of RPP is the difficulty performing the procedure on patients with very large prostate glands and a narrow pelvis. Because of the small incision, glands  $>120$  g can be difficult to resect, particularly if associated with a narrow pelvis; however, glands  $>180$  g have been removed via this approach.<sup>20</sup> A good rule of thumb is that if the base of the gland is not palpable on rectal examination, or if the gland fills the pelvis from side to side, it may foreshadow a difficult resection. Perhaps the most significant disadvantage of RPP is that the current generation of urologists lack familiarity with the perineal technique.

### **Preoperative preparation**

Although the incidence of rectal injury is quite low in skilled hands, RPP does require extensive dissection near the rectal wall. Therefore, we routinely perform a mechanical bowel preparation and provide antibiotic prophylaxis for all patients. A well-tolerated cleansing that avoids enemas includes a clear liquid diet the day before surgery, 45 ml oral buffered sodium biphosphate, and 1 g of erythromycin and neomycin as described by Nichols et al.<sup>21</sup> Preoperatively, a single intravenous dose of cefazolin 1 g is given. Since we transfuse  $<1\%$  of our RPPs, type and cross, or even, type and screen are usually not performed. In addition, we do not routinely recommend autologous blood donation to our patients because of its cost and because it is seldom needed.

### *Anesthesia*

This procedure has been performed using a variety of anesthetics, ranging from a spinal or epidural to general endotracheal anesthesia. We routinely have all of our patients undergo a general anesthetic, as we have found that spinal anesthesia is often incomplete and, perhaps more importantly, the patients are prone to move during the surgery.

*Patient positioning*

For ideal operative conditions to be met, the patient must be placed in an exaggerated lithotomy position with the buttocks brought down slightly beyond the end of the table. Lower-extremity elastic compression stockings (TED hose) are placed, although, because of positioning, the venous drainage of the lower extremities is already maximal. The legs are then secured in Yellofins stirrups (OR Direct, Acton, Massachusetts) and elevated into the lithotomy position. Once the legs have been elevated, the foot of the bed is lowered completely. The perineum is then elevated to a position essentially parallel to the floor by placing rolled blankets underneath the sacrum. When properly positioned, the scrotum should fall forward onto the abdomen and the surgeon should have excellent access to the anal verge (Figure 41.2). All pressure points are well padded. The arms should be abducted as little as possible to prevent injury to the brachial plexus. Once the patient is properly positioned, broad tape is attached to the stirrups and placed over the buttocks to maintain this position. In



**Figure 41.2** (A and B) Patient positioned in the exaggerated lithotomy position with Yellofins stirrups. Note that after proper positioning, the perineum is parallel to the floor.

addition, we routinely place a loose belt across the abdomen to prevent patient migration during the operation. The hair of the posterior scrotum and perineum is shaved and an antiseptic surgical scrub is performed.

*Special instruments*

- Young retractor.
- Lowsley retractor.
- Thorek scissors.

Special instruments (Figure 41.3) greatly facilitate this procedure but are not required. The most useful of these are the prostatic retractors designed by Young and Lowsley. Both of these retractors allow for manipulation of the gland during various portions of the

operation. In addition, Thorek scissors aid in dissection of the bladder neck and the vascular pedicles during dissection under the pubic bone. Another instrument we find particularly useful, but not mandatory, is a multifunction self-retaining retractor, such as the Thompson perineal retractor.



**Figure 41.3** From top to bottom: Lowsley retractor, Young retractor, and Thorek scissors. Although not essential for RPP, each greatly facilitates the procedure.

## Operative procedure

### *Incision*

Prior to incision, the Lowsley prostatic retractor is placed in the bladder and the wings opened. An inverted U or horseshoe-shaped incision is made just inside the ischial tuberosities (Figure 41.4). The apex of the incision is typically located 2–3 cm anterior to the anal verge; usually, a color change in the skin denotes the proper location. The vertical arms of the incision lie medial to the ischial tuberosities and are extended posteriorly to a point lateral to the sphincter at the 3 and 9 o'clock positions. The incision can be carried further posteriorly without side-effects if large flaps are needed. The incision is then carried down 1–2 cm into the subcutaneous fat.

The ischiorectal fossa is developed next. Small stab incisions are made through the ischiorectal fascia bilaterally at the superior aspect of each vertical arm of the incision. Once a defect has been created, these spaces are developed bluntly with the index fingers directed inferiorly and perpendicular to the floor (Figure 41.5). The spaces are opened

with electrocautery. Once the pockets have been adequately developed, the index fingers are brought together toward the midline. A space is then created under the central tendon connecting the ischiorectal fossae. This space overlies the anterior rectal wall and is superior to the anal sphincter. The central tendon is then divided with cautery (Figure 41.6). At this point, the rectum is draped out of the field by applying four Alice clamps to the developed flap and attaching them to a  $\frac{3}{4}$  inch surgical drape.

### *Rectal mobilization*

After division of the central tendon, the rectal sphincter will be seen as an arch overlying the rectum. Dissection is then carried out between the longitudinal rectal fibers on the ventral aspect of the rectal wall and the external anal sphincter. We prefer a modified Belt approach, as described by Hudson and Lilien, whereby bilateral spaces are created through the mid-portion of the sphincter with the remaining central tendon between the two (Figure 41.7).<sup>22</sup> This allows the external anal sphincter to be lifted up and away from the underlying rectum. A Young prostatic bifid retractor is then placed beneath the sphincter and the external anal sphincter is elevated superiorly (Figure 41.8). Using the nondominant hand, two of the previously placed Alice clamps are grasped in the palm while the index finger is placed into the rectum. This allows for downward traction on the rectum. The remaining central tendon is sharply incised with Metzenbaum scissors (Figure 41.9).

The longitudinal fibers of the rectum are then followed to the rectourethralis muscle, which attaches the rectum to the posterior urogenital diaphragm. The depth of dissection is greatly facilitated by the finger in the rectum to constantly monitor the level of resection relative to the anterior rectal wall. The rectum can be mobilized on either side of the rectourethralis with blunt dissection to the level of the prostatic apex. The rectourethralis itself is variably developed, ranging from a few rudimentary fibers to a substantial fibromuscular structure several centimeters long. Once thoroughly isolated, the muscle should be divided sharply, as blunt dissection will invariably result in rectal injury.



**Figure 41.4** Line of incision marked on the perineum. The apex of the incision lies ~2 cm anterior to the sphincter and the lateral wings lie within the ischial tuberosities. A slight change in skin color denotes the area and is marked by the arrow.



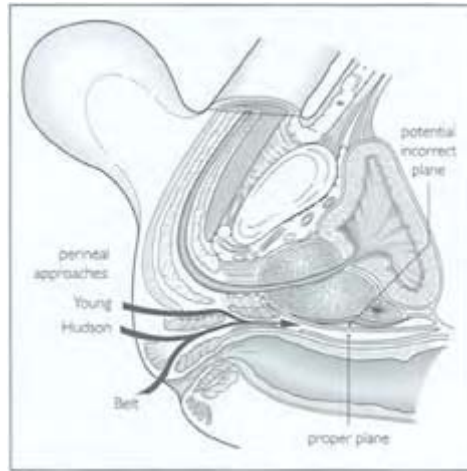
**Figure 41.5** Development of the ischiorectal fossa using blunt dissection. Note the direction of dissection should be inferior and perpendicular to the floor.



**Figure 41.6** The central tendon has been isolated and is elevated away from the underlying rectum prior to its division with electrocautery

After division of the rectourethralis, the Thompson perineal retractor is placed (Figure 41.10).

At this point the ventral rectal fascia should be visible, and is identified by its white, shiny appearance. The space between it and the rectal wall should be developed and can usually be done with gentle, blunt finger dissection. It is important to note that the plane of dissection changes at this point to the vertical from the horizontal. The space must be developed to the base of the prostate, which is identified by palpation of the wings of the retractor. The rectal wall is then gently retracted with a padded retractor to provide optimum exposure. At this point the decision must be made whether to proceed with the nerve-sparing technique or with wide dissection. The posterior lamella is



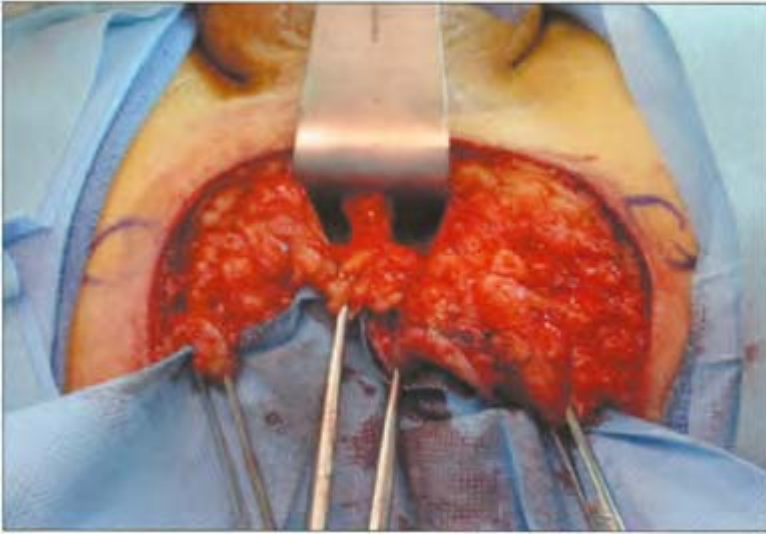
**Figure 41.7** The three described perineal approaches to the prostate. The Young approach is the most direct, but risks injury to the urinary sphincter. The Hudson and Belt approaches allow for early visualization of the longitudinal fibers of the rectum. The anterior wall of the rectum can then be followed directly to the prostate.

the key, and how it is handled from this point forward will define each separate technique. If a nerve-sparing technique is to be used, the fascia should be incised vertically, and the neurovascular bundles mobilized. If extended dissection is intended, the neurovascular bundles can be ligated at their superior edge and the fascia incised transversely to free the rectum (Figure 41.11).

#### *Extended dissection*

The intent of the extended dissection lies not only in the removal of the neurovascular bundles but also in the widest possible resection of the posterolateral fascia. It may be performed either unilaterally or bilaterally. If a unilateral technique is employed, a vertical incision should be made in the ventral fascia just off midline on the side and medial to the neurovascular bundle to be spared. Entry into Denonvilliers' fascia should be avoided. If a bilateral extended dissection is performed, the ventral fascia should be maintained. The fascia is opened transversely at the level of the membranous urethra and the base of the prostate if possible. The neurovascular bundle is then ligated at both ends, and the dissection continued laterally to the base of the bladder.





**Figure 41.8** The external anal sphincter has been entered on both sides of the remaining central tendon and is elevated away from the field with a Young bifid retractor.



**Figure 41.9** The central tendon is sharply divided with Metzenbaum

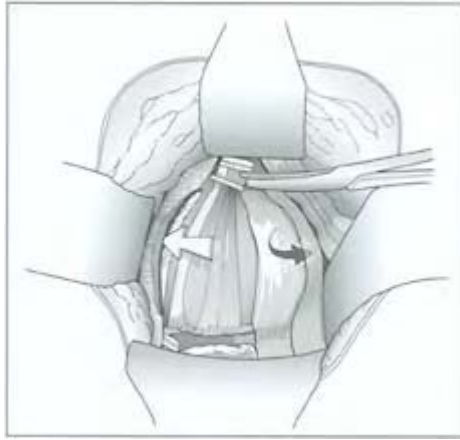
scissors. Note a finger of the non-dominant hand in the rectum, which is used to direct the underlying rectum away from possible injury.

*Nerve-sparing technique*

The key to a nerve-sparing technique lies in the understanding that this dissection is carried out in a plane completely different from the one dissected in the extended approach. Preservation of the neurovascular bundles demands a dissection plane that is inside the ventral rectal fascia of Denonvilliers' fascia. Once the



**Figure 41.10** The Thompson perineal retractor has been placed. We use a grooved retractor superiorly, two 1 inch double-angled retractors laterally, and a 1/2 inch malleable retractor inferiorly. This provides optimum exposure.



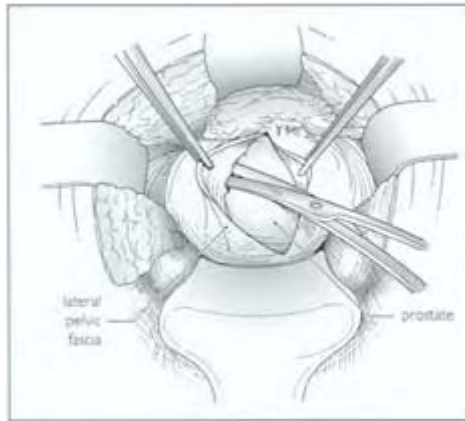
**Figure 41.11** An extended dissection has been performed on the right. The ventral rectal fascia and neurovascular bundle have been clipped and divided at the base of the prostate. The lateral rectal fascia has been incised, exposing the proper plane for a wide dissection (white arrow). The left neurovascular bundle and ventral rectal fascia have been mobilized off of Denonvilliers' fascia, exposing the proper plane for a nervesparing technique (black arrow).

rectum is mobilized, the neurovascular bundles can be visualized running within the lateral aspect of the ventral rectal fascia. If a bilateral dissection is to be carried out, a vertical incision should be made in the midline. If one intends a unilateral dissection, the incision should be made 1 cm lateral to the midline on the side to be saved. The medial edge of the divided fascia is then carefully elevated and separated from the underlying prostatic capsule (Figure 41.12). Perforating vessels usually found entering the prostate from the neurovascular bundles at the superior and inferior neural pedicles are ligated with clips. The neurovascular bundles must be mobilized at least 1 cm over the membranous urethra and sufficiently proximal to the base to ensure enough laxity as to avoid traction injury during removal of the gland. The dissection is then continued laterally and ventrally on the prostatic capsule beneath the dorsal venous complex.

#### *Apical dissection*

Blunt and sharp dissection is continued until the junction of the membranous urethra and apex of the prostate are visualized (Figure 41.13). The urethra is then surrounded by a

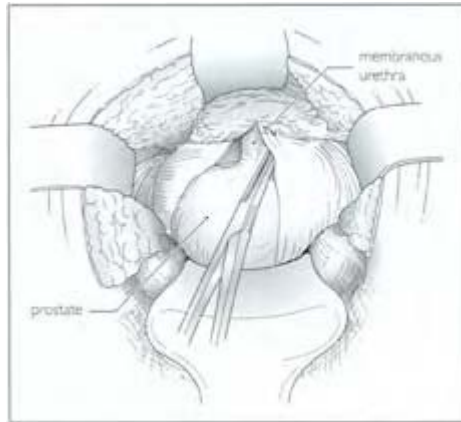
right-angle clamp and hemitransected with a scalpel. At this point we preplace the posterior anastomotic sutures at the 4, 6, and 8 o'clock positions with 2-0 Monocryl. Next, the Lowsley retractor is removed and the remainder of the urethra is sharply transected. The Young prostatic retractor is then placed through the prostatic urethra directly into the bladder and the blades are extended.



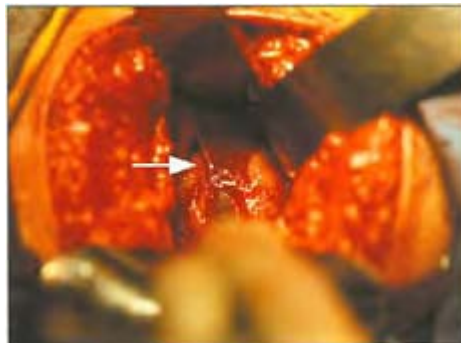
**Figure 41.12** Here the periprostatic fascia (ventral rectal fascia) is split in the midline and a plane developed between it and the capsule of the prostate. The neurovascular bundles course within this fascia.

#### *Puboprostatic ligament division*

The Young retractor is used as the prostate is rotated ventrally to expose the anterior prostatic capsule and the puboprostatic ligaments that lie in the midline beneath the dorsal venous complex (Figure 41.14). It is advisable to divide the ligaments sharply since they are avascular, and this helps to avoid a potential tear in the prostate capsule



**Figure 41.13** Meticulous dissection reveals the junction of the membranous urethra and the prostatic apex. Here the nerves have been spared on the left side and a wide dissection performed on the right. The right-angle clamp should be kept in close approximation to the urethra to avoid injury to the overlying neurovascular bundle.



**Figure 41.14** The Young retractor is used to rotate the prostate ventrally, which exposes the puboprostatic ligaments (arrow). They are avascular and thus can be sharply divided.

from traction and a positive anterior margin. Dissection is carried back until one can readily visualize the circular fibers of the bladder neck (Figure 41.15). Troublesome bleeding from the dorsal venous complex can be handled by grasping the offending vessels with vascular forceps and cauterizing. Generally, however, oozing is handled by placing an open gauze sponge against the plexus and compressing it with a retractor until the prostate is removed. Bleeding is minimal and controlled with pressure and has usually ceased after removal of the prostate.

#### *Bladder neck division*

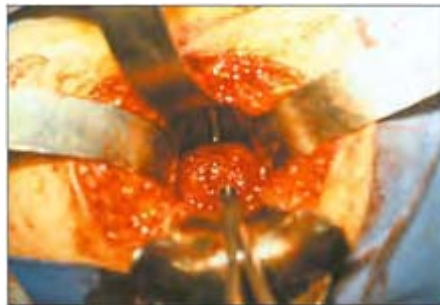
Typically, the muscles of the bladder neck are easily visualized and can be transected with the Thorek scissors. Routine wide excision is not advisable, as cancerous invasion of the bladder neck is rare (3%) and invariably associated with positive margins at another site.<sup>23</sup> The correct plane of transection is identified by palpating the contour of the gland and visualizing the circular fibers of the bladder neck. The anterior bladder neck is transected by cutting down onto the Young retractor until urine begins to flow out of the incision. The Young retractor is removed and subsequent traction applied with the assistance of a inch Penrose drain, which is passed through the division between the base of the prostate and the bladder neck and brought out through the apex of the prostate using a right-angle clamp (Figure 41.16). The posterior bladder neck is then divided using Thorek scissors. Next, attention is turned to the vascular pedicles, which serve as the primary attachments that restrict mobilization of the gland (Figure 41.17). The pedicles are carefully isolated with a right-angle clamp and ligated with surgical clips using a right-angle clip applier. Care is taken to avoid the overlying neurovascular bundles if a nerve-sparing technique was performed.

#### *Seminal vesicle dissection*

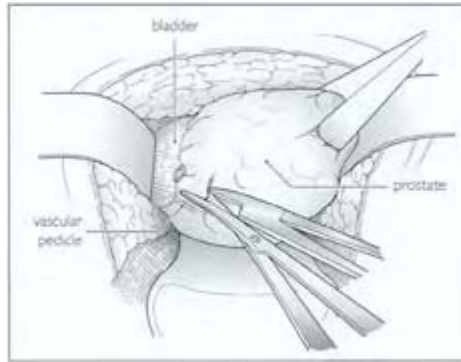
With the majority of attachments released, the prostate is now anchored only by the seminal vesicles and ampulla of the vas deferens. An Allis clamp is placed through the prostatic urethra and clamped to provide better posterior exposure. The prostate is then elevated anteriorly so the seminal vesicles may be approached posteriorly. The respective ampulla and seminal vesicle are isolated, ligated with surgical clips, and transected (Figure 41.18). Once this step is complete, the prostate is handed off the surgical field and the anastomotic repair begun.



**Figure 41.15** The circular fibers of the bladder neck (arrow) are readily seen after division of the puboprostatic ligaments. Thorek scissors are then used to cut down onto the Young retractor and open the bladder.



**Figure 41.16** Here the anterior urethra has been divided and a right-angle clamp has been placed through the prostatic urethra to grasp a 1/4 inch Penrose drain. The drain will be passed through and used for retraction.



**Figure 41.17** The vascular pedicle has been isolated with a right-angle clamp and clipped.



**Figure 41.18** The prostate is reflected anteriorly with an Alice clamp to aid in posterior dissection of the seminal vesicles and ampulla of the vas deferens. Here, the ampullae have been ligated, leaving only the seminal vesicles intact.



*Vesicourethral anastomosis*

The bladder neck is carefully inspected and trimmed as needed. A 20F Silastic catheter is placed in the urethral stump, and 2-0 Monocryl sutures are placed from the urethral stump at the 10 and 2 o'clock positions into the anterior bladder neck at the 10 and 2 o'clock positions and they are snapped to the drape for later use (Figure 41.19). The catheter is then advanced into the bladder. Redundant posterior bladder neck is closed vertically in a racquet handle technique with interrupted 2-0 chromic sutures. Because of excellent exposure and direct visualization, it is unnecessary to evert the mucosal edges prior to anastomosis. At this point the preplaced posterior sutures are placed through the bladder neck. The anastomosis is then completed by tying all sutures down in a sequential



**Figure 41.19** The 20F Silastic catheter is seen exiting through the membranous urethra. The bladder neck is identified by the solid arrow. At this point we place our anterior anastomotic sutures through the membranous urethra (white arrows) and directly into the bladder neck (yellow arrows). The catheter is then advanced into the bladder and the bladder neck reconstructed.

fashion, beginning anteriorly and ending with the posterior sutures.

*Closure*

Because unrecognized rectal injuries are associated with significant morbidity, we routinely place a finger in the rectum prior to closure to ensure there are no proctotomies. If encountered they should be repaired using a standard two-layer closure with 3-0 Vicryl for the mucosa and 3-0 silk Lembert sutures for the seromuscular layer. A 1/2 inch Penrose drain is placed anterior to the rectal surface and brought out through one of the corners of

the incision. The perineal wound is closed in three layers. The perineal body is reconstituted, connecting the deep and superficial portions of the muscle with 2–0 chromic suture. The subcutaneous perineal fascia is closed with interrupted 2–0 chromic suture and the skin edges approximated with 2–0 chromic horizontal mattress suture (Figure 41.20). The sutures should be kept on the outside of the wound. We leave tails of approximately 1 inch to prevent complaints from the patients about the sutures bothering them. Others have described closing the skin using a subcuticular suture, but we find that the horizontal mattress is better as it provides more support at the apex of the wound where a breakdown is likely to occur.



**Figure 41.20** Final closure of the wound with interrupted 2–0 chromic sutures in a horizontal mattress. Note the Penrose drain exiting from the lateral aspect of the wound.

### Postoperative care

We have developed a postoperative pathway for RPPs at our institution (Table 41.1). Clear liquids are given to the patient immediately postoperatively, and the diet is advanced to regular the following morning. Patients are out of bed the evening of surgery and ambulate on postoperative day 1. The Penrose drain is usually removed on the first postoperative day. Ketorolac is routinely given for analgesia and, more times than not, patients do not require narcotics, although they are available as part of our routine postoperative orders. Young, healthy patients are usually discharged within 24 hours, and 95% will be out of hospital by day 2. Nothing is given per rectum. Patients are discharged

home with prophylactic antibiotics while the catheter is in place, and the catheter is typically removed 10–14 days after surgery.

## Complications

### *Proctotomy*

Rectal injuries are generally not problematic if they are noted at the time of surgery, are repaired intraoperatively, and the patient has undergone a bowel prep.<sup>24</sup> We repair the injury with a two-layer closure of 3–0 Vicryl for the first layer, followed by 3–0 silk Lembert stitches for the second layer. The wound is then copiously irrigated with 1 liter of antibiotic irrigation. We perform a two-finger anal dilation to reduce sphincter tone. Large rectal tears, prior radiation, or unprepped bowel are best managed with diverting colostomy. This is generally performed laparoscopically with the assistance of a general surgeon. If a rectal injury has occurred, broad-spectrum antibiotics covering both aerobic and anaerobic bacteria are given for 48 hours. We use the combination of ceftriaxone (rocephin) and metronidazole (flagyl) at our institution. A low-residue liquid diet is encouraged for 5 days. Unrecognized injuries will usually present within the first

**Table 41.1** *Radical perineal prostatectomy postoperative clinical pathway*

|                   | Pre-admission                           | Day of surgery   | Post-op day 1                            | Post-op day 2   |
|-------------------|---|--|--|---|
| Treatment and lab | CBC, Chem 7, UA<br>EKG<br>CXR           | bilat SCDs at all times<br>IS q1°<br>RA SaO <sub>2</sub> ≥92%<br>Foley to DD<br>Penrose—leave in<br>'NPR' sign above bed<br>change perineal dressing pm<br>promise pants on at all times | H&H this AM                              | d/c Penrose after 1 <sup>st</sup> BM<br>Sitz bath after 1 <sup>st</sup> BM          |
| Diet              | clear liquids to start with bowel prep  | sips of clears   | advance to regular                       | regular   |
| Activity          |   | OOB to chair for 30 min this night   | OOB must walk 4 times a day              | OOB and walking D/C home  |
| Meds              | Fleet's<br>Phosphosoda<br>Nichol's Prep | IVF as maintenance<br>mg IV×48° Levsin 0.125 mg<br>PRN Colace 100 mg BID<br>Ancef 1 gram IV×3 doses<br>Percocet 1–2 q4° PRN  | HLIV start<br>PO Abx at dinner           | D/C IV PO pain meds<br>only cont Levsin PRN<br>cont Colace D/C home<br>with PO meds |
| Patient education | Review clinical pathway                 |  | leg bag & catheter care<br>perineal care | review D/C instructions   |
| Discharge         |   | begin D/C planning and   | continue                                 | Discharge home  |

planning

assessing home needs

assessing  
home needs

CBC, Complete blood count; UA, urinalysis; EKG, electrocardiogram; CXR, chest x-ray; SCD, sequential compression device; IS, incentive spirometry; RA, room air; DD, dependent drainage; NPR, nothing per rectum; OOB, out of bed; IVF, intravenous fluids; D/C, discharge H&H, hemoglobin and hematocrit; HLIV, heparin lock IV.

few days and are manifest as fecal drainage from the perineal wound. These are best treated by reopening the incision and repairing the rectum. If the injuries present later, it may be advisable to proceed with a diverting colostomy.

### *Catheter displacement*

If the Foley catheter should fall out in the first 4–5 days, it can usually be replaced by careful passage of a catheter with a coude tip. Any resistance or catheter displacement in the first few days is best handled by cystoscopic replacement of the catheter. After the first week, if the catheter falls out we leave it out and have rarely had any complications.

### *Vesicourethral-perineal urine leak*

This is usually the result of disruption of the racquet handle closure of the posterior bladder neck secondary to bladder spasm. These invariably resolve with prolonged catheter drainage and should be monitored with intermittent cystograms to insure complete healing prior to catheter removal, especially in the case of a salvage prostatectomy. If an anastomotic perineal fistula occurs, replacing the catheter for an additional week has corrected the problem in all cases.

### *Fecal soilage*

This particular complication was not reported until recently. In 1998, Bishoff et al reported this complication in a study of 1200 patients.<sup>25</sup> Each had been mailed a 26-question quality of life instrument to assess fecal and urinary incontinence after prostatectomy. The instrument used was not a validated tool for clinically localized prostate cancer patients. Of the 1200 patients surveyed, 907 returned the surveys; of these, 784 came from patients who had undergone RRP and 123 came from patients who had undergone RPP. In their investigation, Bishoff et al discovered a higher incidence of fecal incontinence (daily, weekly, monthly, or less than monthly) after RPP than after RRP (3, 9, 3, and 16% compared with 2, 5, 3, and 8% ( $p=0.002$ )). In addition RPP patients were more likely to wear pads ( $p=0.013$ ), experienced more accidents ( $p=0.001$ ), had larger volumes of stool leakage ( $p=0.002$ ), and had more loosely formed stools ( $p=0.001$ ).

These data are contrary to the experience at our institution. We recently mailed the UCLA-RAND Prostate Cancer Index, a validated questionnaire, to 184 patients (107 RRP and 77 RPP). This was not a randomized comparison, and the patients were not matched. The survey was completed by 76/107 RRP patients (71%) and 58/77 RPP patients (75.3%). Of interest is the information relayed from the patients regarding bowel

function. When asked if they never or rarely experienced rectal urgency, 31.5% of RRP patients and 20.6% of RPP patients answered positively. Furthermore, 85.5% of RRP and 82.8% of RPP patients reported no bowel-related quality of life effect due to the procedure. To provide a wider perspective, two surgeons with extensive experience in performing RPP were contacted. Dr David Paulson at Duke University has performed over 2000 RPPs and has not seen fecal soilage or incontinence except in those patients previously irradiated prior to salvage perineal prostatectomy. Dr Robert Gibbons from Virginia Mason states that only 1–2% of patients experience fecal soilage, and he has not seen fecal incontinence in any of his patients.<sup>7</sup>

The actual prevalence of this problem remains debatable. Nevertheless, we do routinely counsel patients regarding this potential complication prior to RPP, with the qualifier that it has been reported but that we have not experienced the problem in our practice. Further investigation is certainly warranted, since it was originally reported to occur in both RPP and RRP patients. We are, accordingly, reviewing a large longitudinal database to assess the incidence, prevalence, and severity of fecal incontinence after radical prostatectomy.

#### *Lower extremity neuropraxia*

This is a unique morbidity associated with the perineal approach and is due to positioning. The etiology is presumed to be undue pressure on the sural nerve due to pressure points just lateral to the head of the fibula. Price et al reported that 43 of 111 patients undergoing RPP experienced some degree of lower extremity neuropraxia, although it was of short duration and in all cases resolved.<sup>26</sup> Typically, patients complain of 2–3 days of sensory loss in the leg or foot and may have associated paresthesias. Until 2 years ago we experienced similar problems at our institution. At that time we began using Yellofins Stirrups and have not had a problem subsequently. These stirrups provide superior padding and eliminate any pressure points at the knee in contrast to the conventional Allen or candy-cane stirrups.

#### **Comparison of RPP to RRP**

Few studies can be found that directly compare the results of RRP to RPP. One of the first reports comparing the two techniques was from Boxer et al in the late 1970s.<sup>27</sup> The study involved 329 patients, with 265 undergoing a perineal approach and 64 cases undergoing a procedure performed retropubically. The study was flawed by inconsistencies with pelvic lymphadenectomy and perioperative estrogen therapy, but overall, when the morbidity associated with the two techniques was directly compared, the only difference noted was that the RRP group had an EBL 700 ml greater than the RPP group.

A study by Frazier et al provided the first contemporary analysis directly comparing the two techniques.<sup>28</sup> The population consisted of 122 patients undergoing RPP vs 51 with RRP. The particular technique chosen depended upon surgeon preference. An extensive number of variables were reviewed, including operative time, transfusions, length of hospital stay, length of catheter drainage, both short- and long-term

complications, and evidence of disease extension. Of note, no difference were found between the two groups with regard to positive margins, urethral or bladder neck involvement, and short- vs long-term complications. The only statistically significant differences noted were an increased EBL and a greater number of transfusions associated with RRP. Critics of this study are quick to point out that patients were not matched based upon preoperative data and that, while all RPPs were performed by a single surgeon, the RPPs were divided amongst three.

Haab et al published results of a similar, but smaller study soon thereafter.<sup>29</sup> This study evaluated 71 patients with clinically localized prostate cancer: 35 patients underwent RPP vs 36 undergoing RRP. Each group had similar age, preoperative PSA, and clinical stage. Measured variables included operative time, blood transfusions, length of hospital stay, complication rates, incontinence, sexual function, and pathologic extent of disease. Ultimately, the only statistical differences noted were a higher transfusion rate with the retropubic approach (100% with RRP vs 54% with RPP) and the number of anastomotic strictures (2 in the RRP and 0 in the RPP). Organ-confined rates, incontinence, and PSA failures were similar in the two groups. The authors concluded that the two techniques were identical in their ability to control organ-confined disease.

The largest comparison trial to date was reported by the Uniformed Services Urology Research Group.<sup>30</sup> This study pooled data from five military installations and identified 1698 men who had undergone radical prostatectomies between 1988 and 1997. Of these 1382 underwent RRP and 316 were treated by RPP. In order to provide a more meaningful comparison, patients were retrospectively stratified according to race, clinical stage, Gleason sum, and preoperative PSA. A total of 190 patients were identified in each group who met matching criteria. Data points examined included age, race, PSA, Gleason sum, clinical stage, pathologic stage, EBL and transfusion rate, organ-confined rate, margin positivity, PSA failures, and short- and long-term complications.

No significant differences were noted in matched patient characteristics such as race, mean preoperative PSA, or clinical stage between the patient populations. Overall, the authors found no statistical differences in either PSA failures, margin-positive, or organ-confined rates in this matched group analysis. The only significant differences found were higher EBL in the RRP group ( $p<0.001$ ) and a higher rectal injury rate in the RPP group ( $p=0.03$ ). No differences were noted in regard to incontinence, impotence, bladder neck contractures, or other postoperative complications.

## Conclusion

In this modern era of minimally invasive urology, radical perineal prostatectomy holds great promise. It is a timetested surgical technique with well-proven cancer control rates and both short- and long-term complication rates comparable to those with the retropubic approach. As with laparoscopic procedures, patients are generally in the hospital for a very short stay and are quick to return to their daily activities. It provides an attractive alternative to the laparoscopic approach.

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## Laparoscopic radical prostatectomy

Bertrand Guillonnet and Tullio Sulser

### Introduction

The first laparoscopic radical prostatectomy was performed by Schuessler et al in 1992.<sup>1</sup> It took 6 more years for this technique to become standardized, and reproducible, owing to the strong commitment of several French teams. This approach is now used worldwide by many urologic teams, and thousands of patients have been operated on laparoscopically for treatment of localized prostate cancer. This chapter summarizes the outcomes data on the application of laparoscopic prostatectomy for localized prostate cancer.

### Operative technique

#### *Specific contraindications*

There is no strict anatomic specific contraindication for laparoscopic radical prostatectomy. There are certain case scenarios that will potentially make this operation more difficult.

From the anatomic point of view, a high body mass index (BMI >30) definitively makes this procedure more difficult. The distance to the operative field is greater than the length of standard laparoscopic instruments available, and often necessitates increasing the number of access ports.

A large prostate (>60 g) makes lateral prostatic dissection more difficult secondary to poor vision, particularly when the pelvis is deep and narrow. Moreover, large glands often have a prominent prostatic median lobe that makes bladder neck dissection difficult.

A previous history of prostate surgery (transurethral incision of the prostate, transurethral resection of the prostate or even open prostatectomy) is not a contraindication for the laparoscopic approach but it does make the surgery more difficult. Finally, previous history of intraabdominal surgery can potentially preclude the transperitoneal route, making the extraperitoneal route the preferred method.

#### *Preoperative care*

Antibiotic prophylaxis, by a single intravenous dose of third-generation cephalosporin is initially prescribed 2 hours before the operation.

Prevention of thrombosis remains an essential element of perioperative care. Compression stockings are mandatory during the surgery and hospital stay. Bowel preparation with or without oral antibiotic is optional and dependent on surgeon preference.

### *Installation*

Positioning of the patient is an essential step of the procedure. The surgeon should supervise all the steps of position to prevent positioning injuries.

The patient is placed in the dorsal supine position and secured to the operative table via a thoracic wrap of elastic adhesive tape. The arms are abducted along the body in a way to avoid risk of brachial plexus injury, while the legs are positioned in a modified frog-leg position with foam support. Generous padding of the lower extremities is recommended to prevent muscular ischemic injury to the calves. The buttocks are positioned at the end of the operative table to allow for intraoperative rectal and urethral access.

Standard skin preparation is carried out from the costal margins to the perianal region. The patient is draped medially, with each leg draped individually. An 18F Foley catheter is inserted on the sterile field and the bladder is drained.

The monitor is placed between the patient's legs, as close as possible to the surgeon's eye level. A right-handed surgeon stands on the patient's left with his assistant on the opposite side. The scrub nurse stands on the surgeon's left with the instrument table.

After inferior umbilical incision, a Verres needle is introduced intraperitoneally. Insufflation is started after confirmation that the needle is within the abdominal cavity. A 10 mm trocar is then inserted into the umbilicus for passage of the 0° laparoscopic lens. The patient is repositioned in the Trendelenburg position, so as to improve the access to the pelvic region, with spontaneous gravity mobilization of the intestine and sigmoid colon. The operating table is lowered to an ergonomic position for the surgeon.

Four other 5 mm trocars are inserted: one into the left lower quadrant, one in the midline half-way between the umbilicus and the pubis, one at the level of the umbilicus in the mid-clavicular line, and one in the right lower quadrant at McBurney's point. The surgeon uses the two upper ports close to the camera port in order to have a triangular approach to the operative field. The assistant has at his disposal the lateral right and the suprapubic ports (Figure 42.1).

### *The operative technical steps*

Transperitoneal pelvic lymph node dissection is performed according to the usual<sup>2</sup> or the extended lymph node dissection.<sup>3</sup> As to our experience, the number of removed nodes was 19 (range 6–42), the mean operative time for the extended lymph node dissection was 55 (37–73) min, and no complications occurred (Figure 42.2). A descriptive narrative of pelvic lymph node dissection is given in Chapter 40.

Six standardized steps can be individualized during laparoscopic radical prostatectomy.<sup>4</sup>



**Figure 42.1** Four 5 mm trocars are used for instrumentation. The individual surgeon works with two trocars on each side of the scope in order to optimize the triangulation of his instruments. The scope is held by a voice-controlled robotic arm, allowing the assistant to assist with both hands.



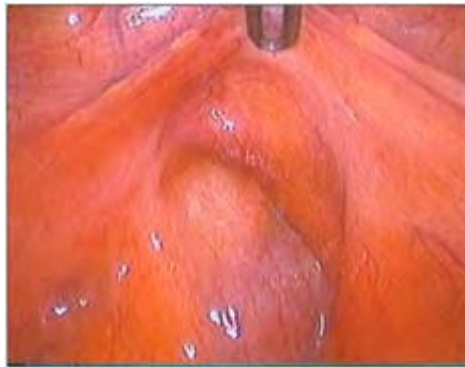
**Figure 42.2** After the extended lymph node dissection is performed, the left external iliac artery, hypogastric artery, obturator nerve, and the ureter are clearly visible.

### First step: posterior approach to the seminal vesicles

**Incising the pouch of Douglas.** The sigmoid colon may be held gently by the assistant, retracting the rectum cranially. The surgeon will then notice the appearance of two peritoneal arches in the pouch of Douglas. The superior one represents the approximate location of the ureters and the trigone. The inferior arch, just above the peritoneal reflection, is created by the merger of the vasa deferentia in the midline.

The posterior peritoneum is incised transversally along the inferior peritoneal arch (Figure 42.3). The dissection follows the inferior peritoneal flap and enters into an avascular plane that should be developed. This exposes Denonvilliers' fascia, which is easily recognizable by vertical fibers.

**Freeing the seminal vesicles.** Once Denonvilliers' fascia is identified, the outlines of the seminal vesicles and vasa deferentia are clearly visible. Denonvilliers' fascia is transversally incised, allowing for clear identification of the vasa deferentia, which are coagulated with bipolar forceps and then transected. One must be aware of the presence of the deferential artery of the vas that runs along the vas and that must be carefully coagulated. Transection of the vasa deferentia provides for direct access to the seminal vesicles. They should be dissected along their surface to isolate the two vascular pedicles, one at the tip and the second at the base. These arteries are meticulously coagulated by bipolar forceps to prevent thermal injury of the neurovascular bundle (Figure 42.4). The vesicles are then completely mobilized to their respective bases.



**Figure 42.3** The assistant holds up the bladder to facilitate opening of the pouch of Douglas. The seminal vesicles are revealed, generally 2 cm above Douglas' pouch, recognizing an arch.



**Figure 42.4** The seminal vesicles are located immediately behind the peritoneum. This direct access leads to a close dissection of the seminal vesicles complex. The entire surrounding vascular network is clearly visible, allowing for precise dissection with minimal damage to the nervous plexus when a nerve-sparing technique is considered.

**Opening Denonvilliers' fascia.** Incision of Denonvilliers' fascia allows an easier and safer dissection later in the operation, by separating the rectum away from the prostatic pedicles. To facilitate the exposure, the assistant can, by pulling the vasa deferentia upward, place Denonvilliers' fascia on tension. It will appear to have longitudinal striations under the magnification of the laparoscope. Denonvilliers' fascia is then incised medially and horizontally on the line of reflection between the prostatic base



**Figure 42.5** Holding up the seminal complex reveals Denonvilliers' fascia, which is transected transversally,

### demonstrating the prerectal fat and the posterior aspect of the prostate.

and the posterior surface of the seminal vesicles. As soon as a shallow incision is made, prerectal fat is revealed (Figure 42.5).

No attempt is made to dissect the prostatic apex from this posterior approach. Further dissection is not necessary and can be dangerous, since the rectum appears usually vertical. In case of difficulties differentiating the rectum, the use of a Hegar bougie inserted into the rectum is helpful, to improve tactile perception of the anterior rectal wall.

### Second step: anterior approach to the prostate

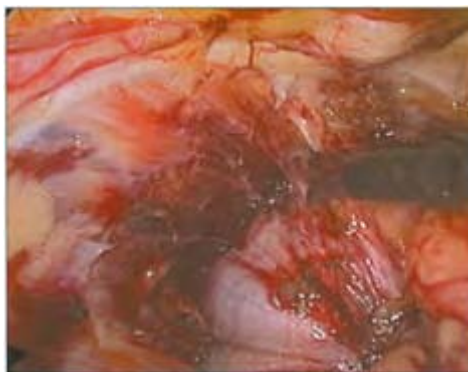
**Entering Retzius' space.** The bladder is filled with approximately 120 ml of saline to help identify the contours of the bladder. The anterior parietal peritoneum is incised from one umbilical ligament to the other just above the distended bladder. If a lymph node dissection has been performed, it is easier to follow the pubic bone that is already exposed to enter Retzius' space, and then to transect the umbilical ligaments as high as necessary; otherwise, the medial umbilical ligaments are preserved. By staying close to the medial aspect of the medial umbilical ligaments and heading medially, the pubic arches are encountered. This dissection allows for clear identification of the urachus that is divided last, thus minimizing the risk of injuring the bladder. It is essential to free the bladder well from its anterior and lateral attachments in order to create a large working space and to permit a tension-free vesicourethral anastomosis at the end of the operation. After the bladder is freed anteriorly and laterally, it is emptied with a syringe. Since the patient is in Trendelenburg position, spontaneous emptying is never complete.

**Exposing the endopelvic fascia.** The fat over the fascia covering the prostate must be gently swept away in order to clearly expose the intrapelvic fascia and the puboprostatic ligaments (Figure 42.6). The superficial dorsal vein is identified and coagulated with bipolar forceps. The endopelvic fascia is visualized lateral to the prostate, and incised at its



**Figure 42.6** After developing the space of Retzius, the endopelvic fascia is opened (here on the left side) and the fibers of the levator ani are pushed

away to free the lateral aspect of the prostate.



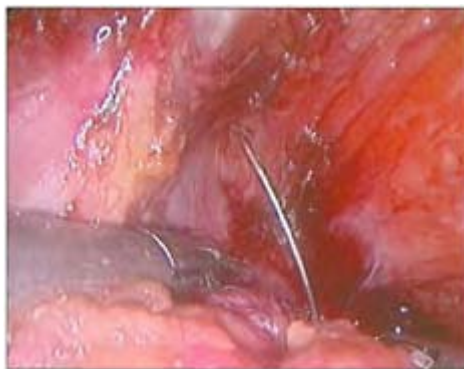
**Figure 42.7** Towards the apex, the fibers of the external sphincter are freed from the prostate, preserving them as much as possible. This operative maneuver reveals the lateral and inferior aspects of the deep venous prostatic complex.

line of reflection with the pelvic floor muscles (Figure 42.7). An adherent zone between the muscle and the prostate is often found. These attachments correspond to vascular penetration. The veins, once identified, are coagulated and transected, allowing complete opening of the area lateral to the apex. Occasionally, an artery runs cephalad to the veins, which is preserved, since it runs toward the sphincter complex. Incision of the puboprostatic ligaments is done under visual control, taking care to avoid the veins of Santorini's plexus. The endopelvic fascia incision can be extended toward the fascia that covers the veins laterally. This lateral incision will facilitate further dissection and exposure of the dorsal venous complex.

**Ligating the dorsal venous complex.** Santorini's plexus is ligated with a 2–0 absorbable suture, passed with a # 26 needle underneath the venous plexus from one side to the other of the distal side of Santorini's plexus (Figure 42.8). For a right-handed surgeon, the needle is passed from the right side of the plexus to the left side with backhand, the needle being situated such that the curve of the needle follows the curve of the symphysis.

Depending on the size of the plexus, a second separate suture or a figure-of-eight stitch may be placed to make the ligation more hemostatic. At this point of the operation, transection of the complex is unnecessary and will be done later.

A back-bleeding stitch, ligating the preprostatic venous drainage, is placed, since it is helpful during the subsequent bladder neck dissection and section of the venous complex.



**Figure 42.8** The venous complex is ligated with a 2-0 SH stitch under close vision (here from the right to the left side).

### **Third step: bladder neck dissection**

This step is considered the most difficult since the anatomic landmarks are not well defined. To identify the bladder neck area, the anterior prevesical fat must be retracted superiorly, causing a faint outline of the prostatovesical plane. The cranial retraction of the preprostatic fat is possible because the superficial dorsal vein had been previously transected. The prostatic vesical junction is generally located where the fat becomes adherent. The fascial covering at this point is transversally incised at this landmark, which needs coagulation of several veins running in this layer.

It is then generally easier to find an avascular plane between bladder and prostate that is developed by sharp and blunt dissection. The prostatic urethra is identified by a change in the orientation of the muscular fibers, which become longitudinal rather than circular. The urethra is dissected laterally on each side. The bladder is checked again to be empty and the catheter balloon is deflated.

The urethra is incised transversally and the tip of the catheter is pulled up by a grasper via the suprapubic port, to expose the posterior urethral wall that is incised at the level of the bladder neck (Figure 42.9). Since the bladder neck is thus preserved, the ureteral orifices are far away from the bladder incision and are not specially identified. While the assistant pulls up the prostate via the catheter, the surgeon exposes the posterior face of the bladder neck, grasping the posterior bladder incision.





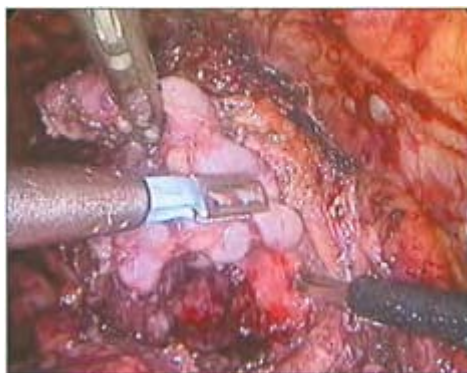
**Figure 42.9** After opening the bladder neck, the superficial layer of Denonvilliers' fascia should be opened to create access to the already freed seminal vesicles. A grasper holds up the posterior aspect of the prostate while the scissors retract down the posterior wall of the bladder neck, revealing Denonvilliers' fascia, already open here.

As one proceeds to incise the posterior junction between the prostate and the bladder, it is important to direct the dissection straight posterior, following the posterior bladder wall. This way one enters the 'anterior layer' of Denonvilliers' fascia. This fascia is recognized by the vertical muscular fibers between the prostate base and the bladder neck. The fascia is incised in order to gain access to the previously dissected retrovesical space. The vasa deferentia and the seminal vesicles are then simply brought into the operating field by the assistant. This maneuver exposes both sides of the prostatic pedicles, since they have been already completely dissected medially and laterally (Figure 42.10).

#### **Fourth step: lateral dissection of the prostate**

**Preserving the neurovascular bundles: the intrafascial technique.** The assistant grasps the vas and the seminal vesicle through the space of dissection between the prostate and the posterior bladder neck, and pulls them upward.

The inferior and medial landmarks are identified by the posterior layer of Denonvilliers' fascia that had been already dissected during the first step of the procedure. The superior and medial landmarks require making an incision in the periprostatic fascia, on the prostate, from the base toward the apex (Figure 42.11).



**Figure 42.10** The direct access to the seminal vesicles exposes the pedicle of the prostate (here the right side) where the seminal vesicle is grasped and held up. The lateral part of Denonvilliers' fascia is visible and should be incised to identify safely the medial aspect of the neurovascular bundle (here on the right side).



**Figure 42.11** The perforating vessels should be identified accurately before any transection. Here, a pedicle artery is coagulated with slender bipolar forceps on the prostate side, far removed from the neurovascular pedicle to avoid thermal injury.

Finally, the medial landmark requires the transection of the prostatic pedicle. This is made easier by the previous dissections that exposed the pedicle high on the prostate, theoretically at a safe distance from the nervous and vascular components of the bundles. Due to the magnification, the pedicle vessels are well visualized and must be systematically controlled (Figure 42.12). Because of the traction on the seminal vesicles, the vessels appear to rise vertically, which facilitates their exposure but is a distortion of their natural orientation. One must remember that the neurovascular bundles are attached. It could be helpful



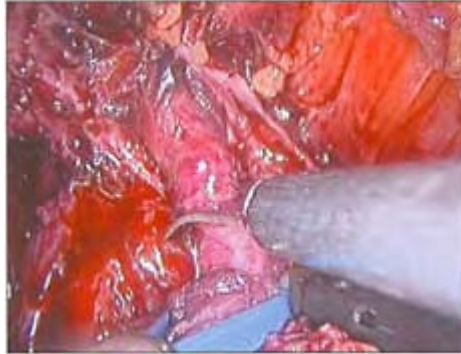
**Figure 42.12** The neurovascular bundle (here on the left side) is freed all along the prostate. Particular attention is paid to the apex where the bundle could be very close and adherent to the apical edge of the prostate.

for the surgeon to reorientate himself periodically during the dissection of the pedicles to keep the location of the posterolateral neurovascular bundle in view.

Once the pedicle is transected, the two fascial incisions (the superior, periprostatic, and the inferior, Denonvilliers' fascia) can be joined. It is then possible to develop, with careful and blunt dissection, an avascular intrafascial plane of the periprostatic (lateral prostatic) fascia pushing the neurovascular bundle lateral and posterior (Figure 42.13). Thus, the incision/dissection of the periprostatic (lateral prostatic) fascia displaces the neurovascular bundle away from the lateral prostatic pedicle. This intrafascial dissection is extended toward the apex. Depending on the size of the gland, dissection is more difficult at the distal third of the gland as it approaches the bladder neck. It is preferable to continue the apical dissection of the bundle after transecting Santorini's plexus and the urethra, which gives mobility to the gland and facilitates the exposure of the distal third of the prostate. At the apex, the neurovascular bundles are divergent from the prostate, but must be followed until their entrance into the pelvic floor, below and lateral to the urethra, to avoid the risk of injury. Due to the magnification, the pulses of the arterial

component of the bundle are often visible, which could be a good anatomic guide to the functional integrity of the bundle. Hemorrhage around the bundles is always minor and, for the sake of neurovascular integrity, should not be controlled.

**Non nerve-sparing procedure.** If nerve sparing is not considered, the procedure is easier. The prostate pedicles are transected far from the prostate and the posterolateral attachments of the prostate are not dissected but simply controlled (by bipolar coagulation or clips) and transected.



**Figure 42.13** Once the bundles are freed and away from the urethra, the latter is transected.

It is important to remember that, if this step looks easier, the risk to enter into the rectum is higher because the dissection is performed close to it, in the perirectal fat.

#### **Fifth step: apical dissection of the prostate**

At this time, only three structures are attached to the prostate: Santorini's complex, the urethra, and the rectourethralis muscle.

**Sectioning the dorsal venous complex.** Because the superficial dorsal vein has been ligated and the pedicles have been controlled, there is little bleeding when the dorsal complex is incised. The incision is tangential to the prostate to avoid capsular incision at this place. Gradually, the dorsal vein complex is retracted anteriorly to reach an avascular plane of dissection, situated between the venous complex and the urethra. This plane must be developed to perfectly expose the anterior and lateral urethral wall.

**Incising the urethra.** Laterally, the urethra must be dissected free from surrounding fibrotic structures. A Béniqué catheter (metal sound with an 'S' shape) is introduced to tactilely identify the urethra. The urethral wall is then incised with scissors or a retractable cold knife. The urethral bougie is pushed through the anterior urethrotomy and into the pelvis to expose the lateral and posterior urethral walls (Figure 42.14). The posterior wall of the urethra is similarly incised with scissors.



**Figure 42.14** Particular attention is required for the transection of the posterior wall of the urethra, to avoid any opening into the posterior aspect of the prostate that could lead to positive margins or incomplete resection of the prostate.

**Transection of Denonvilliers' fascia.** After complete transection of the urethra, the distal attachment of Denonvilliers' fascia is on stretch and represents the final attachments of the prostate. In order to avoid injury to the neurovascular bundles, it is necessary to cut these fibers from lateral to medial. This division of the distal part of Denonvilliers' fascia close to the prostate completely frees the specimen, which is placed into a laparoscopic bag (Figure 42.15), under the control of a 5 mm scope through a lateral port.

The specimen is then extracted through an enlargement of the 10 mm umbilical incision, depending on the size of the specimen. The gland is macroscopically checked, and sent to the pathologist for frozen section if necessary. The umbilical incision is carefully closed around a 10 mm trocar and the abdomen is reinsufflated.

#### **Sixth step: urethrovesical anastomosis**

Eversion of the bladder mucosa and reconstruction of a wide bladder neck, traditionally performed during open radical retropubic, are not necessary during laparoscopic prostatectomy. However, occasionally, reconstruction of a very large bladder neck is necessary to make the anastomotic approximation smaller and more continent, and a posterior tennis racquet rather than an anterior racket is performed. This maneuver moves the ureteral orifices away from the suture line.

Throughout this portion of the procedure, the surgeon works with two needle-holders. The anastomosis is made with interrupted stitches of 3-0 absorbable suture with a



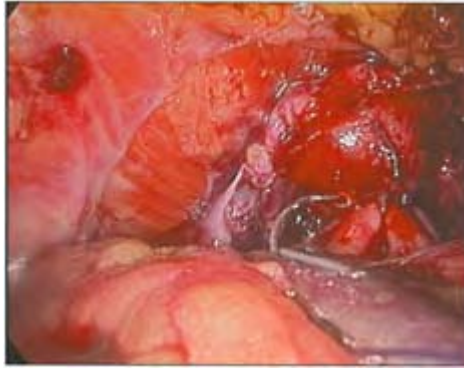
**Figure 42.15** After completion of the prostatectomy, the specimen is extracted in a laparoscopic bag through an enlargement of the umbilical incision. The operative specimen is inspected to rule out positive margins.

#18 mm half-circle needle. All ties are made intracorporeally. The metal sound (Béniqué catheter with a depressed tip) helps to guide the needle into the urethra and to place the sutures, at precise locations around the urethra (Figure 42.16).

The three first sutures are placed posterior at 5, 6, and 7 o'clock, going inside-out on the urethra and outside-in on the bladder neck. The 5 o'clock stitch goes inside-out on the urethra (right hand, forehand) and outside-in on the bladder (right hand, forehand); the 5 and 6 o'clock stitches go inside-out on the urethra (right hand, forehand) and outside-in on the bladder (left hand, forehand). These stitches are tied intraluminal.

Four other sutures are symmetrically placed at 4 and 8, then 2 and 10 o'clock, and tied outside the lumen. As a rule, for a right-handed surgeon, the right-sided stitches go outside-in on the bladder (right hand, forehand) and inside-out on the urethra (left hand, backhand); the left-sided stitches are symmetrical, going outside-in on the bladder (left hand, forehand) and inside-out on the urethra (right hand, backhand).

Three final anterior stitches are placed at 11, 12, and 1 o'clock, symmetrically to the posterior stitches. The 11 and the 12 o'clock stitches go outside-in on the urethra (right hand, forehand) and inside-out on the bladder (right hand, forehand), while the 1 o'clock stitch goes outside-in on the urethra (right hand, forehand) and inside-out on the bladder (left hand, forehand). Once the stitches are tied, the Foley catheter is inserted. The bladder is filled with 180 ml of saline to check the water tightness of the anastomosis and to confirm the correct position of the catheter. Finally, the balloon is inflated with 10 ml.



**Figure 42.16** Performance of the anastomosis is facilitated with the use of a 'Béniqué bougie'. This device directs the anastomotic needle to encompass the full thickness of the urethra.

### Completing the operation

The abdominal pressure is lowered to 5 mmHg, to check for venous bleeding. The peritoneal incisions are left open and two suction drains are placed, one anteriorly in Retzius' space and one posteriorly through the incision of the pouch of Douglas, on contact with the rectum. The 5 mm trocars are removed under visual control and are checked to exclude vascular injury, particularly of the epigastric vessels. Finally, the incisions are conventionally closed and dressed.

### *Operative variants*

#### Technical points

**Extraperitoneal approach.** The extraperitoneal approach has been described<sup>5,6</sup> and is currently used by several teams. The theoretical advantages are the absence of risk of injury of intra-abdominal organs, less peritoneal irritation, and a quicker development of Retzius' space. On the other hand, the operative room is narrower, reducing the ergonomic conditions of the procedure. During this procedure, posterior mobilization of the bladder is not as great as with the transperitoneal approach, making the anastomosis much more difficult, with tension that necessitates some technical tricks (anterior and/or posterior racquet stitches to reconstruct the bladder neck). But, above all, it appears that a key point of the nerve-sparing operation lies in the initial approach to the seminal vesicle, since the seminal vesicles complex is more easily accessible via the transperitoneal

approach, thus potentially preserving the neurovascular bundles better than the extraperitoneal approach.

**Operative strategy.** Different strategies have been developed, mainly with a direct approach to Retzius' space without preliminary dissection of the seminal vesicles complex.<sup>7</sup> The theoretical objection is the same as for the extraperitoneal approach, if a nerve-sparing procedure is planned. The retrograde technique of retropubic prostatectomy,<sup>8</sup> mimicking Walsh's technique, has been described, but doesn't seem to have the advantage of the benefit of an axis of dissection identical to the vision. However, this technique has proven to have excellent results for preserving the neurovascular bundles via the traditional open approach. If the laparoscopic counterpart can replicate the open approach, this may become the preferred approach.

*The anastomosis:* The urethrovessical anastomosis can be correctly performed with a running suture, and several teams prefer to use a continuous suture rather than an interrupted one.<sup>9</sup> An advantage of the interrupted sutures is that they are theoretically less ischemic, they can always be done in all situations, the help of the assistant is not necessary, and the manipulation of short stitches is easier when one starts. On the other hand, a running suture needs less knots, and could be a simpler way for the less experienced surgeon.

### The trocars

**Placement of trocars.** The trocars can be placed in any array, according to the habits of the surgeon. In particular, they can be arranged 'like a fan' round the umbilicus, with two trocars in the left iliac fossa and two trocars in the right iliac fossa. In the absence of an arm holding the camera, this set-up is certainly more surgical assistant-friendly, since the assistant is not bothered by the surgeon's movements. It allows the surgeon to operate seated, with the two trocars in front of him, but is theoretically less ergonomic since the triangular operating range of the instruments is reduced. The dissection on the opposite side of the prostate can be impractical, and the sutures necessitate modifying the instrument set-up anyway into a triangular configuration.

**The size and number of the trocars.** Except for the umbilical port, an additional 10 mm port is not always necessary. In addition to the 10 mm trocar for the scope, four other ports are sufficient.

### Instrumentation

The use of various different instruments is technically possible. In particular, endoscopic staplers can be used for transection and hemostatic control of the prostatic pedicles when a non-nerve-sparing procedure is planned.<sup>7</sup> Apart from the cost, the major critical point is that the rectum can be pulled into the line of section.

The use of harmonic scissors is advocated to theoretically decrease the extent of the heat diffusion at the level of the capsular arteries and thus protect the neurovascular bundles from thermal injury. With the same goal, the use of clips to control pedicular vessels has been advocated.

Outcome data are not presently available to confirm this theoretical advantage over bipolar coagulation.



### The use of the 'robotics'

**Voice-controlled robotic arm.** The use of a voicecontrolled robotic arm enables the surgeon to control the laparoscopic lens. This device allows the surgical assistant to fully assist the primary surgeon and also ensures excellent stability of the image.

**Remote-controlled laparoscopic surgery.** The feasibility of a remote robotic device to perform laparoscopic radical prostatectomies has been demonstrated and confirmed by several teams.<sup>10-12</sup> Although this technology may enable an experienced surgeon to perform this complex procedure from a remote site, the increased cost and legality of this form of telesurgery has not been worked out.

### *Postoperative care*

#### Analgesics

The usual analgesic protocol for the first 24 hours consists of anti-inflammatory drugs. Often no intravenous analgesia is requested by the patient from the second postoperative day. Major analgesics are rarely necessary; in those cases postoperative complications must be suspected and ruled out.

#### Nutrition

Oral intake is usually resumed 12 hours after the operation and intravenous perfusion is generally stopped between the 12th and 24th hour after operation.

#### Antithrombosis care

Antithrombosis precautions are of major importance given the increased risk of a pelvic cancer operation and a laparoscopic approach, which diminishes the venous return to the heart. Preoperative and postoperative prevention is based on thrombosis prophylaxis started before the operation (low molecular weight heparin) and continued for 2 weeks after the operation in the form of compression stockings while in hospital and early mobilization of the patient on the first day after operation. This essential preventive element is favored by the absence of postoperative pain, allowing for early mobility.

#### Bladder catheter removal

As a rule, if the bladder neck has been preserved and if the anastomosis was watertight during the operation, the bladder catheter can be removed as early as the 3rd day after operation. If the quality of the anastomosis is uncertain, the bladder drainage should be prolonged. In such a situation, a cystogram is necessary to assess the anastomotic integrity. The Foley catheter must not be removed if urine is present in the pelvic drain.

## Technical feasibility

### *Surgical conversion*

Surgical conversion to a conventional open retropubic approach can be indicated in case of intraoperative complications and/or technical difficulties.

The intraoperative complications are generally due to hemorrhage of Santorini's venous plexus. In this event, vascular control should be attempted by compressing the plexus with a clamp and placing a new ligature. From our experience, the use of bipolar coagulation or the application of a clip is a transient and unsatisfactory solution. If hemostasis seems impossible and if the decision to convert is taken, it is always possible to compress the plexus with a laparoscopic clamp or by the insertion of a sponge through the 10 mm trocar to compress the bleeder, while the laparotomy is performed.

Dissection planes that are difficult to identify may result in technical problems. This can be potentially due to an extracapsular tumor (pT3 or pT4) adhering to the posterior surface of the prostate, which may make the posterior dissection plane difficult. Dissection planes are difficult to define in patients treated with prior endocrine therapy. The prostate is of reduced size, with ill-defined surgical borders. Another cause of operative difficulties may be a history of prostatic surgery: transurethral resection of the prostate (TURP) or open prostatectomy. Obviously, the preservation of the bladder neck in these cases is impossible.

The patient needs to be informed beforehand that there is always a risk of open surgical conversion. Although the conversion rate decreases with experience and now tends towards zero, there will always be difficult cases for which laparoscopic surgery cannot be completed. One must keep in mind that the surgical benefit is for the patient and the primary goal is patient safety.

Finally, it is important to stress the technical difficulty of a correct and watertight urethrovesical anastomosis. When the urethrovesical anastomosis cannot be achieved correctly, a minilaparotomy must be done to perform the anastomosis in the conventional way, and take advantage of the incision to extract the operative specimen.

### *Operative time*

Laparoscopic prostatectomy is an ambitious operation that makes high demands on the technical skills and anatomic knowledge of the surgeon. At the end of the operation the anastomosis is a very important surgical step, always difficult, that determines the quality of the postoperative results. Obviously, with experience, the surgical time decreases. At present, the mean operative time reported by several different teams is around 200 min, which is more or less comparable to the operative time required for the retropubic procedure.<sup>4,8,13,14</sup>

## **Specific complications**

Despite the technical difficulties and long learning curve, in our experience the morbidity of laparoscopic radical prostatectomy is low.

### *Hemorrhage*

#### **The dorsal venous complex**

Vascular injury mainly results from the inability to surgically control Santorini's venous plexus. A laparoscopic procedure cannot be continued in case of bleeding as hemorrhage interferes considerably with vision. One needs to revert to conventional surgery if adequate hemostasis cannot be obtained. This complication occurred early in our experience when a secure ligation of the dorsal venous complex was not correctly placed. Presently, control of the venous complex presents no technical problem and is always perfectly performed, according to the technique we have described above.

#### **The epigastric injury**

Another potential vascular injury is to the epigastric artery, which occurs during insertion of the ports. On completion of the procedure, it is essential to carefully examine the point of entry of each secondary sheath into the abdomen. Unrecognized bleeding related to an epigastric injury can lead to an extensive hematoma, requiring transfusion and sometimes even surgical repair.

#### **Transfusion**

Altogether the transfusion rate in many different series is low, and averages less than 5% of the patients.<sup>14,15</sup> This low transfusion rate is clearly related to the reduction of the estimated blood loss to an average of less than 500 ml in these series. There are several explanations for this reduction. The pressure of the pneumoperitoneum (12 mmHg or less) certainly contributes to occlusion of small veins, but the other element concerns the technique itself. Since a laparoscopic procedure cannot be continued in case of insufficient vision, one of the objectives is to ensure excellent vision of the operative site, which requires systematic coagulation of all small vessels that are generally neglected in an open procedure. Finally, the quality of vision is improved by magnification of the operative field and the various camera angles optimizes the visualization of vascular structures.

*Bowel complications***Rectal injury**

Rectal injury may occur during two different steps of the procedure: firstly, when Denonvilliers' fascia is incised too far posterior at the base of the seminal vesicles; secondly, during the lateral dissection of the prostate at the apex, where Denonvilliers' fascia is in close proximity to the rectum and space for dissection becomes limited. In this situation, the use of an intrarectal bougie may facilitate optical and tactile detection of the plane of Denonvilliers' fascia as well as the limits of the rectal wall. In our experience, all cases of rectal injury occurred at the end of the procedure during transection of the distal attachments of Denonvilliers' fascia, when the dissection of the posterior aspect of the prostate was not completed. Once the injury is recognized, it can be accurately repaired with two layers of suture line. This can be meticulously achieved laparoscopically, and colostomy is not required. The operative site should be disinfected, and antibiotic therapy prescribed. Oral intake is delayed (after the 3rd day) and the bladder catheter should be removed on the 8th postoperative day. A cystogram should be obtained to confirm a watertight anastomosis.<sup>16</sup>

**Peritonitis**

This is related to unrecognized bowel injury. Although this trauma is rare, it requires immediate diagnosis and treatment.<sup>17</sup>

*Urologic complications***Bladder injury**

Bladder injury occurs during the approach to the space of Retzius. Because the bladder extends towards the umbilicus, the urachus must be transected as high as possible. A bladder injury is easily identified (appearance of vascular mucosa; gas in urinary bladder). It is repaired by extramucosal sutures of the bladder. The bladder catheter is left in place for 5 days.

**Ureteral injury**

Ureteral injury can occur during the freeing of the seminal vesicles through the pouch of Douglas, when the peritoneal incision is made too high, and the ureter is mistaken for the vas deferens. This complication is rare. The best way to avoid this complication is to follow the vas to the ampulla and the seminal vesicle, which identifies clearly the structure as the vas deferens. An injured ureter should be accurately sutured via the laparoscope over a ureteral stent, and the healing process checked postoperatively with an intravenous pyelogram (IVP).

The ureter can also be damaged during the closure of the urethral anastomosis. This danger is greater after previous prostate surgery (TURP or open prostatectomy) or a large median prostatic lobe. To prevent this complication, indigo carmine should be utilized to identify the ureteral orifice. Laparoscopic reintervention may be necessary to correct this problem.

### **Urinary fistula**

Urine in the pelvic drains documents anastomotic leakage. A few milliliters of urine by suction drainage frequently subsides within 24 hours and has no sequelae. Large amounts of urinary drainage, however, may cause clinical signs of a urinoma in the peritoneal cavity (rising serum creatinine, metabolic acidosis, decreased urine output). During these situations, the bladder catheter is left in place until urine drainage from the pelvic drains is zero. The Foley catheter can be removed after a radiologic control documents an intact anastomosis.

Performing a new anastomosis due to a persisting fistula is sometimes necessary, particularly when a ureteral orifice is inadvertently included in the anastomosis. This secondary anastomosis can be successfully performed laparoscopically without difficulties.

### **Anastomotic stricture**

With the present follow-up, only 1 of the patients developed a stricture of the anastomosis that required an additional endoscopic procedure. This stricture resolved after endoscopic incision. Anastomotic stricture after laparoscopic radical prostatectomy is rare in our hands.

### *Pelvic lymph node dissection*

#### **Obturator nerve injury**

One patient developed a mild obturator nerve paralysis, probably secondary to an electrocautery injury. This paralysis resolved spontaneously without sequela in less than 6 months.

### **Lymphoceles**

Lymphoceles are a complication of the pelvic lymph node dissection. They can occur even after a transperitoneal approach. When asymptomatic, they should be neglected, but a surgical intervention is necessary when they are infected or cause compression symptoms to adjacent structures (obturator nerve, bladder, colon). Pelvic lymphoceles are treated by percutaneous drainage and/or laparoscopic decompression. A full review of this technique is given in Chapter 12.

## **Oncologic results**

Oncologic outcomes are based on pathologic examination of the operative specimen and biologic non-progression. Current follow-up of oncology outcomes for laparoscopic prostatectomy are too short; therefore, no definitive advantage between open and laparoscopic prostatectomy can be made.

### *Pathologic evaluation*

The positive surgical margin rate varies widely from one series to another, depending on the population selection, clinical stage, pathologic grade of prostate biopsy, and the experience of the surgeon. In the literature, the overall rate of positive margins after laparoscopic radical prostatectomy ranges between 11.4%<sup>13</sup> and 26.4%.<sup>18</sup>

As demonstrated in other series of radical retropubic prostatectomy,<sup>19</sup> surgical margin status had a significant effect on the biochemical progression-free survival (90% negative vs 67% positive margins at 3 years).<sup>20</sup>

The location of the positive margins with laparoscopic radical prostatectomy is primarily apical (about 50%), as reported in several studies.<sup>20,21</sup>

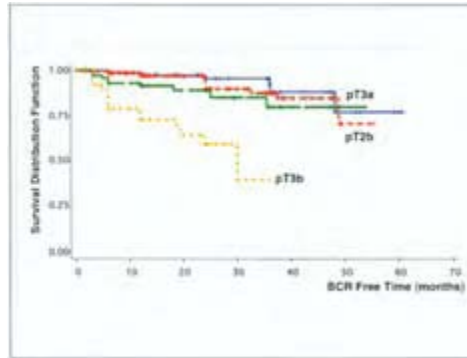
These rates and locations are comparable to what is already reported in large series of contemporary open retropubic radical prostatectomies, suggesting that it is the disease process itself more than the surgery that is involved in these locations.<sup>22,23</sup>

### *Biochemical evaluation*

Preoperative prostate-specific antigen (PSA), pathologic stage, surgical margin status, and Gleason score in the postoperative specimen are factors for cancer recurrence after radical prostatectomy.

The data on the prognostic factors in the laparoscopic series are similar to those previously published for the open retropubic approach. If pathologic characteristics of the surgical specimens are comparable, definitive cure by the two techniques is similar.

At present, the data available for laparoscopic radical prostatectomy calculated overall progression-free survival rate of 90.5% at 3 years (PSA <0.1 ng/ml). According to the pathologic stage, the progression-free survival rate was



**Figure 42.17** Percentage of biochemical progression-free survival (progression=PSA >0.1 ng/ml) according to pathologic stage.<sup>20</sup>

91.8% for pT2aN0/Nx, 88% for pT2bN0/Nx, 77% for pT3aN0/Nx, 44% for pT3bN0/Nx, and 50% for pT1–3N1 ( $p=0.001$ , Figure 42.17).

#### *Clinical evaluation: trocar/operative site tumor seeding*

The question of an additional oncologic seeding related to the laparoscopic technique is controversial but needs to be considered. The majority of prostate tumors are organconfined. Thus, with no direct tumor contact with the pneumoperitoneum, there is little to no risk of tumor dissemination. With this knowledge, the risk of cutaneous tumor seeding is very low in regard to the number of laparoscopic radical prostatectomies performed for prostate cancer throughout the world. This correlates with no reports of seeding from laparoscopic prostatectomy in the world literature.<sup>24</sup>

The question of trocar/operative site tumor seeding from laparoscopy has been extensively examined for renal cancer by many laparoscopic surgeons.<sup>25,26</sup> The risk for tumor seeding to these sites is similar to traditional open renal surgery. Currently, trocar/operative site seeding has not been reported for laparoscopic radical prostatectomy. An incidence of trocar site seeding was reported after laparoscopic pelvic lymphadenectomy for prostate cancer.<sup>24</sup> In this case a large mass of necrotic prostate cancer was inadvertently entered with gross tumor spillage.

#### **Urinary function**

To assess continence rates after radical prostatectomy, a self-administered questionnaire is completed by the patient at home.<sup>27</sup> At present, only preliminary urinary continence outcomes are available secondary to short-term follow-up. Moreover, refinement and evolving operative technique would not allow for long-term follow-up. However, the

experiences of our first group of patients undergoing laparoscopic prostatectomy have sufficient follow-up to access long-term outcomes.

In order to evaluate continence as objectively as possible, we have prospectively evaluated the recovery of urinary control in 530 patients operated upon between January 1998 and December 2002. All patients were followed for a minimum of 12 months. Twenty-three patients were excluded from the analysis due to failure to precisely determine the continence status postoperatively. In 263 patients (53%), the puboprostatic ligaments were partially incised during apical dissection and preserved in the remaining patients according to the surgeon's preference. Urinary control was assessed by the International Continence Society (ICS) male questionnaire completed by patients 6 months postoperatively and reviewed by an independent research specialist. Patients were considered continent when they did not require any protection to keep them dry. Patients who used pad(s) even only for few drops were considered incontinent. At 12 months after laparoscopic radical prostatectomy, 79% of patients ( $n=401$ ) recovered complete urinary control and 92% of patients ( $n=466$ ) were either totally continent or using only one pad per day. Median time to achieve continence was 1.5 months (range 1–18). Patients younger than 70 years were more likely to achieve total urinary control than older patients ( $p<0.001$ ). Clinical and pathologic tumor stage ( $p=0.8$  and  $p=0.7$ , respectively), preoperative PSA ( $p=0.2$ ), prior surgery for benign prostatic hyperplasia (TURP or transvesical prostatectomy) ( $p=0.4$ ), and the development of an early anastomotic leak ( $p=0.2$ ) did not influence the postoperative continence status. Neither the surgical technique used, with or without puboprostatic ligament preservation, nor the quality of neurovascular bundle preservation, affected the continence recovery or time to achieve continence. We assessed the difficulty of the surgery by blood loss, patient BMI, and the specimen's weight. The specimen's weight was the only significant factor associated with postoperative incontinence ( $p=0.02$ ).

Thus, the continence rate on the basis of this definition was 79%, while 13% of patients were using only one pad, which corresponds to a so-called 'social continence' rate of 92%, which is comparable to the continence rate usually found in the literature after the open retropubic<sup>27,28,29</sup> or laparoscopic approach.<sup>30</sup>

### Sexual function

The evaluation of potency is a very difficult task: no scale is appropriate to evaluate sexual function with respect to and taking into account the multiple medical factors.

The nerve-sparing technique is now performed in every case where it is oncologically feasible.

Interposition sural nerve grafting during radical prostatectomy provides a potential pathway to restoring autonomic innervation while providing excellent oncology control of the cancer. Published data have shown a 75% initial success rate after bilateral sural nerve graft interposition, and recovery after unilateral graft interposition with contralateral nerve preservation appears comparable to recovery with bilateral nerve preservation.<sup>31</sup> Tuerk et al. demonstrated the technical feasibility of sural nerve grafting laparoscopically.<sup>32</sup> Furthermore, laparoscopy provides the important advantages of optical magnification with improved visualization in a bloodless field.



Between 2000 and 2002 in our series, 116 patients with a mean age of 59 (44–70) years and with normal preoperative sexual activity were selected for a nerve-sparing procedure and assessed postoperatively with a selfquestionnaire. The rate of erection obtained without any medical assistance ranged from 60 to 80%, and the rate of sexual intercourse, achieved eventually with the assistance of oral drugs, ranged from 33% to 74%, for uni- or bilateral nerve-sparing surgery, respectively. Among the 92 patients with bilateral preservation of the vascular bundle, 52% recovered a potency that allowed satisfactory intercourse in the first 3 months. Some other series confirmed equivalent rates of sexual function when bilateral nerve sparing was technically successful.<sup>21,33</sup>

Since sexual preservation is a critical point, hopefully this rate will improve with time and the quality of erections will allow patients to resume a satisfactory sex life.

This experience supports the fact that anatomic and functional nerve-sparing surgery is technically feasible through a laparoscopic approach with satisfactory results.

### Conclusion

Radical prostatectomy can be performed via laparoscopy in an uncompromising manner. Certainly the laparoscopic technique demands advanced technical skill, knowledge of laparoscopic prostate anatomy, an expertise in prostate oncology, and the support of a whole team involved in the care of patients with prostate cancer.

Laparoscopy offers the patient two kinds of benefits. The first benefit is common to all laparoscopic procedures, i.e. a low intra- and postoperative morbidity, with a shortened convalescence. The second benefit is correlated to the magnified vision and the accuracy of the surgery, which provides good and promising functional results in regards to continence and potency. But most importantly, these advantages are supported by equivalent oncologic outcomes to open retropubic radical prostatectomies. These data, obtained from a few centers, must be confirmed by larger prospective series. If confirmed, laparoscopy will become the approach of choice to perform radical prostatectomy effectively with less morbidity. Like all surgical procedures, laparoscopic radical prostatectomy is still evolving and improving. The present status is the basis for future questions. Therefore, laparoscopy is a step towards improving our knowledge of surgery in the care of patients with prostate cancer.

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## Robotic prostatectomy

Jeffrey Evans, Ashutosh Tewari, Robert Moore, and Mani Menon

### Introduction

Prostate cancer surgical therapy has evolved dramatically since Young's pioneering radical perineal prostatectomy almost 100 years ago. Millin introduced the radical retropubic approach in 1947, but it was not used commonly until the 1970s secondary to complications with hemorrhage, impotence and incontinence. Since that time, significant advances in the understanding of neurovascular anatomy by pioneers such as Walsh have dramatically improved the mortality and morbidity of the procedures. Walsh states that the three goals of the surgeon, in order of importance, are cancer control, preservation of urinary control, and preservation of sexual function.<sup>1</sup> Many urologic surgeons have proposed a fourth, albeit less important consideration, a minimally invasive approach to the operation that would provide a faster recovery with decreased postoperative discomfort.

In efforts to achieve the above stated goals, Schuessler et al described the first laparoscopic radical prostatectomy in 1992.<sup>2</sup> Subsequent efforts have been undertaken by experienced French laparoscopic urologists Guillonnet and Vallancien<sup>3</sup> and others. Unfortunately, these and other authors have reported a very difficult learning curve and positive margin rates of approximately 20%.<sup>3,4</sup> However, they have found that patients treated with this technique have enjoyed similar continence and erectile function rates, with arguably less postoperative discomfort and quicker recovery times.<sup>3-7</sup> The risk of perioperative complications is similar to the open technique.<sup>8,9</sup>

Robots have been utilized to perform repetitive tasks in many industries. Recently, robotic technologies have been adapted for surgery. This technology offers the surgeon the ability to perform complex operative maneuvers, improves surgical precision, optics and camera control, and makes techniques such as suture placement and intracorporeal knotting easier with minimal operative experience. Thus, using minimally invasive surgical robots potentially enables the surgeon to make a smoother transition from an open surgical technique to a minimally invasive one. Robotic assistance offers an open surgeon sophisticated tools to perform complex laparoscopic surgery. This chapter leaves the discussion of standard laparoscopic radical prostatectomy and the use of robotics in urology to other chapters in this book and focuses on the technique of robotic radical prostatectomy using the da Vinci Surgical System (Intuitive Surgical, Inc., Sunnyvale, California). The technique and results reported here are largely based on the experience of the surgical team at the Vattikuti Urological Institute, Henry Ford Hospital. We will also discuss the controversy of such intervention and the feasibility of telesurgery.

## Indications

It is well established that patients with nodal or metastatic disease do not benefit from operative intervention.<sup>10</sup> Patients with locally advanced disease have a significantly worse prognosis and it is imperative that negative surgical margins are obtained. Given the preceding statements, we encourage considering a minimally invasive approach in patients who are suspected of having organconfined disease based on prostate-specific antigen (PSA), Gleason score, and digital rectal examination. Men with Gleason score >5 prostate cancers with a Charlson comorbidity score of <3 are candidates for this procedure.

Patients should be questioned regarding previous abdominal surgery, peritonitis, and orthopedic or neurologic ailments. A history of stroke or cerebral aneurysm is a relative contraindication because the patient will be in pronounced Trendelenburg position for several hours. Previous abdominal surgery is not a contraindication.

## da Vinci Surgical System

The da Vinci Surgical System comprises the surgeon's control console and the surgical arm unit (Table 43.1 and Figure 43.1).

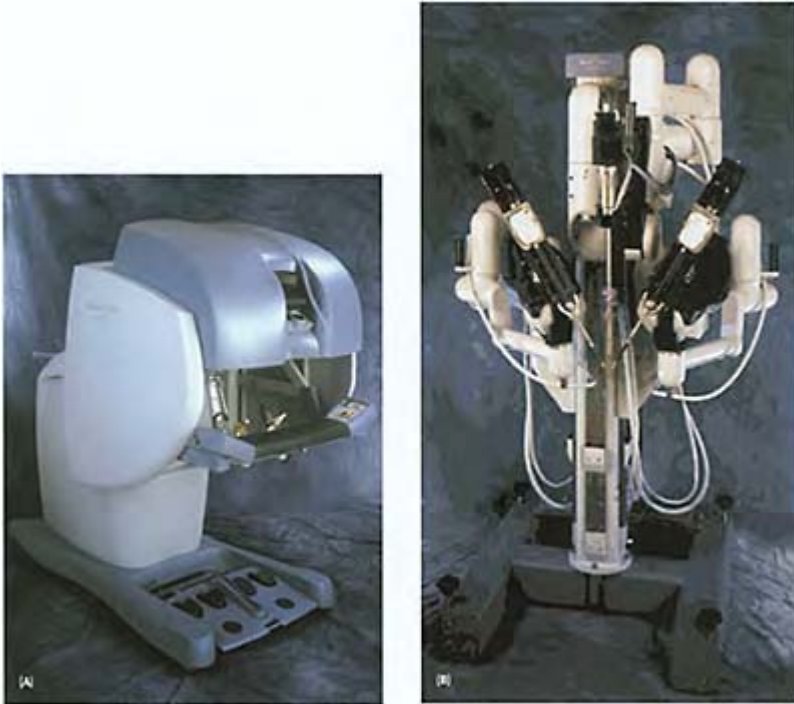
**Table 43.1** *Components of da Vinci Surgical System*

Surgeon's control console:

- Three-dimensional video screen with one monitor for each eye
- Handles/surgical master (adjustment of motion scale: 2:1, 3:1, 5:1)
- Foot controls (camera control, electrocautery/harmonic scalpel, clutch function)

Surgical arm unit:

- Two robotic arms matched to surgical master via 8 mm port (EndoWrist technology with six degrees of freedom)
- One robotic arm for endoscopic camera via 12 mm port (two high-intensity light sources with two charge-coupled three-chip cameras in a single 0° or 30° instrument)



**Figure 43.1** (A) Surgeon's control console and (B) surgical arm unit.

*Surgeon's control console*

The purpose of the console is to provide the surgeon with a sensory experience that is similar to the open surgical approach (Figure 43.1). This is accomplished using a three-dimensional video screen and handles known as the master controls and foot controls.

The optics of the device provide information that is a significant advance over that of the two-dimensional information provided by standard laparoscopy. The endoscope consists of two high-intensity illuminators and two camera devices to provide a high-resolution, three-dimensional image that allows a 5–10 $\times$  magnification, which is determined by the distance of the camera to the object (Figure 43.2).

The camera has 0 and 30° lenses. The 30° lens can be oriented upward or downward for adequate visualization.



**Figure 43.2** A 30° endoscopic camera.

Foot pedals at the console lock and unlock the camera. The hand controls allow precise movement of the camera when the foot pedal is in the unlocked position. Refocusing can also be accomplished with the foot pedals.

#### *Surgical arm unit*

The surgical arm unit consists of three individual devices that control two surgical instruments and the endoscope via input from the hand controls and foot pedals from the surgeon's control console. A variety of surgical instruments are available and are easily interchanged from the surgical arms by the assistants at the operative site (Figure 43.3).

Every motion of the master handles has a response from the 'slave manipulators'. The movements are detected by high-resolution sensors that transfer the movement based on an adjustment motion scale of 2:1, 3:1, or 5:1. This allows for very precise movements by the robot. Additionally, the end effectors of the device increase the degrees of freedom allowed by standard laparoscopy from four to six, aided by the EndoWrist technology, which simulates the action of the human wrist. This can be extremely useful when addressing problematic portions of the operation such as sparing the neurovascular bundles, ligation of the dorsal vein and, most importantly, suturing the urethrovesical anastomosis.



**Figure 43.3** (A) Multiple instruments are available to be interchanged with

the surgical arm unit. These are controlled via the surgical master handles. (B) EndoWrist technology allows increased flexibility and six degrees of freedom.

### **Procedure<sup>11,12</sup>**

#### *Position*

It is imperative to position the patient properly prior to initiating the procedure. The patient is placed in the supine position with adequate padding of the pressure points and shoulder, back, legs, and arms. We use gel pads for the patient's back. Cotton pads are used to protect the axilla and other pressure points. The arms are tucked along the patient's torso and the hands are protected with egg crate foam padding.

The surgical arm unit is quite bulky and must be placed at the foot of the bed for adequate port placement. The length of the arms necessitates either bringing the unit in with the legs splayed laterally or deflecting the legs toward the floor. Care must be taken to adequately pad the lower extremities. The patient is placed in maximal Trendelenburg position to allow the intestines to retract cephalad and provide better pelvic exposure.

#### *Port placement*

Proper port placement is critical to this procedure. Three robotic ports and two standard ports are placed in an infraumbilical position after pneumoperitoneum is achieved with a Veress needle introduced through an upper left abdominal quadrant or umbilical puncture. The da Vinci instruments are placed medially. The 12 mm port for the camera is placed at the umbilicus. The remainder of the ports are placed with the 30° up lens to visualize the abdominal wall. The two 8 mm ports are placed caudal and lateral to the camera to avoid interference. They are inserted approximately 10 cm from the midline on a line joining the anterosuperior iliac spine to the umbilicus. The assistants should place their ports superior and lateral to the da Vinci 8 mm ports. Two additional ports are placed in the right side for retraction, suture placement, and suction purposes by the first assistant. The lateral assistant port is 10 mm and the medial one is 5 mm. A sixth 5 mm assistant port may be placed lateral and slightly inferior to the left robotic port. The last laparoscopic cannula is not essential but facilitates retraction, and forces a sometimes unwilling assistant to participate in the operation.

Space within the narrow male pelvis can be quite limited. It is important to place the ports as high within the abdomen as possible where the abdominal surface is broad. Conversely, it is necessary to ensure that the end effectors can adequately reach the distal-most portion of the prostate where the critical portions of the operation occur such as ligation of the dorsal venous complex, dissection of the prostatic apex, and formation of the urethrovesical anastomosis. The authors feel that this is one of the more difficult portions of the learning curve to master. A gestalt of where to place the instruments,



based on the patient's length and pelvic structure, must evolve with each procedure performed.

### *Assistants and telesurgery*

Communication between the surgeon and the assistants is imperative. Because the surgeon is displaced from the operative field, he is unaware of what is occurring on the operative field and back table. His only sensory input is via the console. His assistants must be vocal. Conversely, the surgeon must direct his assistants clearly. A microphone system is available to the surgeon so that he can be clearly heard without vocal strain. It can be quite frustrating for the surgeon to maneuver around his assistants' instruments in the limited operative field. Also, he depends on the assistants to rapidly change his end effectors and camera smoothly, place suture material into the surgical field, provide adequate suction-irrigation, and for retraction of the bladder and prostate.

Communication is one of the most critical portions of the operation, but it becomes paramount when telesurgery is being contemplated. Remote robotic prostatectomy has not been performed to date, but other remote procedures such as laparoscopic cholecystectomy have been performed with success.<sup>13</sup> This is a tremendous feat of advanced telecommunications with real-time responses from the surgical arm via a remote console. The skills of the surgical assistants in this setting are even more critical, as port placement and possible conversion to an open procedure are mandatory when performing this surgical modality.

### *Surgical steps*

#### **Creation of the working space**

We begin the dissection anteriorly using the 30° lens, looking up. The parietal peritoneum covers the bladder anteriorly and the rectum posteriorly. Between these two structures lie the vasa deferentia, the pelvic vessels, and the distal ureters. The operating surgeon holds the da Vinci long-tip grasper in the dominant hand, and the hook electrocautery in the nondominant hand. The broad, sweeping moves of traditional laparoscopy must be abandoned in favor of fine, finger control. The initial incision is made just above the pubic symphysis. The incision should be low as possible, but high enough to avoid entering the dome of the bladder. It may be useful to start the incision on either side of the medial umbilical ligaments, and to end with urachal transection. The incision is carried down vertically to the vasa, and up to the iliac bifurcation if a lymphadenectomy is being performed. The extraperitoneal space is developed and the bladder is 'dropped' posteriorly.

#### **Lymph node dissection**

A standard pelvic lymphadenectomy is performed using the 30° down lens for visualization. We prefer to use a wide field of vision so that the major vessels are always in the field. A 1:3 scaling is used so that the dissection is more precise.

### **Exposure of the prostatic apex**

We use the 0° lens and a 1:3 nonscaling mode for this part of the operation. The tissue is swept away from the pubic symphysis, exposing the endopelvic fascia and puboprostatic ligaments. The levator fibers are mobilized off the prostate to clear a space around the apex. Several venous tributaries may be encountered in this region and should be controlled with bipolar cautery. We leave the puboprostatic ligaments intact and limit the urethra dissection prior to placement of the dorsal vein stitch. This approach has improved our early continence results, with 90% of our patients being free of pads at 8 weeks.

### **Dorsal vein stitch**

The 0° or 30° up lens are used for the dorsal vein stitch without scaling. We use laparoscopic-length suture (6 inch) on a CT-1 needle (0 braided, polyglactin suture with a 36 mm taper needle; Ethicon, Somerville, New Jersey) to control the dorsal venous plexus with two simple stitches over the urethra and at the mid prostate. The prostatic stitch is placed primarily for traction and rotation of the prostate during posterior dissection, not to decrease back-bleeding.

### **Bladder neck transection**

The 30° 'down' lens gives the surgeon the ability to precisely dissect the bladder neck. The prostatovesical junction is usually at the point at which loose fat can no longer be swept off the prostate. With experience, one can identify a shallow groove between the prostate and bladder and the horizontally oriented detrussor fibers. Sometimes the prostatovesical junction is demarcated better laterally than at the midline. Using the electrocautery hook, the bladder neck is incised to expose the Foley catheter. There should be no oozing at this stage of the operation. If bleeding is present, the surgeon maybe in the prostate. The balloon is deflated and pulled anteriorly toward the ceiling by the assistant to expose the posterior bladder neck. The posterior bladder neck should be incised precisely, maintaining a clear detrussor margin for the subsequent urethrovesical anastomosis. After transecting the posterior bladder neck, the anterior layer of Denonvilliers' fascia is transected. The vas deferens is dissected for about 3 inches and then transected, coagulating its vascular supply. The seminal vesicles are dissected out. The deferential artery and seminal vesicle pedicles (at the tip) are controlled using a wristed da Vinci bipolar forceps. Care is taken to avoid using excessive electrical currents, because the neurovascular bundles lie very close to the tips of the seminal vesicles. The remaining attachments between the bladder and prostate are divided with electrocautery to expose the lateral pedicles of the prostate.

### **Lateral pedicle control and preservation of neurovascular bundles**

Using both blunt and sharp dissection, we expose the lateral prostatic pedicles. Early on in our experience, we controlled the pedicles with ligating clips. However, we have seen 4 patients in whom there was delayed migration of the clips into the urethra. Therefore, the pedicles are dissected until we identify the urethral branches of the prostatic artery.

These run into the base of the prostate and are individually coagulated, preserving the capsular artery. If nerve sparing is planned, we enter the plane between the layers of prostatic fascia and dissect away the neurovascular bundle. We use the articulated robotic scissors to incise the lateral prostatic fascia anterior and parallel to the neurovascular bundles. Once the correct plane is entered, most of the dissection occurs in a relatively avascular plane. Appropriate traction of the prostate is important to identify the correct plane of dissection. This dissection is carried out as far downward as possible and lateral to the convexity of the prostate.

### **Dissection behind the prostate**

Once both the vas deferens and seminal vesicles have been dissected free, they are pulled upward by the left-sided assistant. This maneuver places the Denonvilliers' fascia on tension, and a faint plane between the rectum and prostate is visible. The posterior dissection plane, at least at the prostatovesical junction, is within layers of Denonvilliers' fascia. In this location, the magnified field shows that there are multiple layers of fascia. In conventional radical prostatectomy, this dissection is carried out behind all layers of Denonvilliers' fascia, and between the rectum and the fascia. We were concerned that we may have a high incidence of positive margins with dissection between the planes; however, this has not been the case. Therefore, we continue to dissect in between the layers of Denonvilliers' fascia because it leaves an added protective fascial layer over the rectum. The distal limit of this dissection is the prostatic apex.

### **Apical dissection of the prostate**

We use a 0° lens with 1:3 scaling to incise the dorsal venous complex and urethra. Using an electro-hook or scissors, the prostatic end of the puboprostatic ligaments and the dorsal vein complex are incised perpendicular to the urethra. To minimize the possibility of a positive apical margin, the anterior wall of the urethra is transected with the scissors 5–10 mm distal to the apex of the prostate. The posterior wall of the urethra and the rectourethralis muscle are transected. The freed specimen is then placed in an EndoCatchl (US Surgical Corp., Norwalk, Connecticut) specimen retrieval bag.

In our series, as well as in most open radical prostatectomy series, the most common location of positive margins is at the apex.<sup>14</sup> The articulated scissors and three-dimensional visualization allow precise periurethral biopsies without sacrificing urethral length. These biopsies are sent for frozen section. In the rare instance (5% in our series) that they are found to be positive, additional biopsies are taken from the appropriate location. The above approach decreases positive apical margins significantly.

### **Urethrovesical anastomosis**

The tails of a 6 inch dyed and a 6 inch undyed RB1 (3–0 braided, Monocryl suture on a 17 mm taper needle; Ethicon, Somerville, New Jersey) suture are tied together to create a single 12 inch suture with a knot in the middle and a needle at either end. Using the dyed end, the anastomosis is started by passing the needle from outside in at the 4 o'clock position on the bladder and inside out on the urethra. We continue suturing clockwise

until the 10 o'clock position. The assistant holds the stitch taut. We then start the undyed end of the suture, passing it outside in on the urethra and then inside out on the bladder. This suture is run counterclockwise until the 11 o'clock position. The needles are cut off, and the free dyed and undyed ends are tied together. This stitch allows completion of the entire urethrovaginal anastomosis with a single intracorporeal knot. Importantly, the anastomosis is watertight. A drain is seldom necessary.

### Preliminary results

Data collection is complete on 200 of the first 250 patients who underwent surgery by Dr Menon. Table 43.2 summarizes some of the variables. A Gleason score of  $\geq 7$  for cancer was noted in 57% of patients. The average body mass index (BMI) was high (28); 86% patients had pathologic stage pT2a to pT2b, and the remaining patients were classified as pT3. The mean operative time was 160 min and the mean blood loss was 153 ml. No patient required intraoperative blood transfusion and the mean postoperative hematocrit value was 39%.

Table 43.2 also lists the perioperative complications. The port-site hernias and ileus were seen in our earlier cases. We have had 1 ileus and no hernias in the last 150 cases. The return of sexual function was also evaluated. We noted that at 6 months, 82% men who were <60 years old had return of sexual function and 64% had sexual intercourse. Additionally, 96% of patients were either free of having to wear pads or were using a liner for security reasons, and 4% were using  $\geq 1$  pads. Patients who were dry or using a liner were 'mostly satisfied' to 'delighted' with the quality of life because of urinary symptoms, whereas those wearing pads were 'mostly dissatisfied' or 'unhappy' with the quality of life. Forty patients were discharged within 4–6 hours after surgery.

### Discussion

The advances in treating prostate cancer over the last 100 years are astounding. Many feel that robotic prostatectomy is the next evolution in surgical therapy of this condition. There is no debate that significant advances have been made in robotic technology, and that this procedure is technically feasible and possibly comparable to the open technique in regards to outcome. However, some argue that the expense involved, difficult learning curve, and arguably modest benefit in hospital stay make this modality unnecessary.<sup>15–17</sup> Some people consider robotic prostatectomy is nothing more than a marketing scheme.<sup>17</sup> We acknowledge the concerns of these authors, but we and other authors feel that this technique holds promise and warrants more investigation.<sup>18–24</sup> The enhanced visual acuity, precision movements afforded by the adjusted motion scaling, six degrees of freedom available with EndoWrist technology, and ability to aid practitioners with less experience from a remote location are very attractive features of any robotic procedure. Prospective randomized trials of open, standard laparoscopic and robotic prostatectomy will answer this controversy, but we are doubtful that they will ever be done, given patient and surgeon emotions. Perhaps a prospective cohort study of results obtained by

expert surgeons, using a common approach to evaluate outcomes, may prove to be a surrogate for randomized trials.

**Table 43.2** *Baseline, operative, oncologic, and postoperative variables (single team's experience of first 200 cases)*

| Variable  | Value                    |
|---|--------------------------|
| Age (years), mean $\pm$ SD (range)                      | 59.9 $\pm$ 7.1 (42–76)   |
| BMI, mean $\pm$ SD (range)                              | 27.7 $\pm$ 2.8 (19–38)   |
| Serum PSA (ng/ml), mean $\pm$ SD (range)                | 6.4 $\pm$ 2.47 (0.6–41)  |
| Clinical Stage, <i>n</i> (%):                           |                          |
| T1c   | 80 (49.7)                |
| T2a   | 17 (10.6)                |
| T2b   | 64 (39.6)                |
| Gleason score (biopsy), <i>n</i> (%):                   |                          |
| 6   | 135 (66.5)               |
| 7   | 56 (27.6)                |
| 8   | 8 (3.9)                  |
| 9   | 4 (1.9)                  |
| Pathologic stage, <i>n</i> (%):                         |                          |
| T2a   | 28 (14.7)                |
| T2b   | 137 (72.1)               |
| T3a   | 13 (6.8)                 |
| T3b   | 12 (6.3)                 |
| Gleason score (histopathologic specimen), <i>n</i> (%): |                          |
| 6   | 86 (43)                  |
| 7   | 92 (46)                  |
| 8   | 16(8)                    |
| 9   | 6 (3)                    |
| Specimen weight (cm <sup>3</sup> )                      | 45.3 $\pm$ 12.3 (18–122) |
| Percentage cancer, mean $\pm$ SD (range)                | 19 $\pm$ 9.8 (1–80)      |
| Node status (%)   | 0.5                      |
| Positive margins (%):                                   | 6                        |
| Focal   | 5                        |
| Extensive   | 1                        |
| Operative time (min), mean $\pm$ SD (range)             | 160 $\pm$ 28 (71–315)    |
| Intraoperative blood loss (ml)                          | 153                      |
| Blood transfusions (%)                                  | 0                        |
| Mean hemoglobin at discharge (g/dl)                     | 13                       |
| Pain score on first postoperative day                   | 3                        |
| Variable  | Value                    |
| Catheterization time (days)                             | 7                        |
| Hospital days   | 1.2                      |
| Undetectable postoperative PSA at 6months (%)           | 92                       |

|   |       |
|---|-------|
| Discharge within 24 hours (%)                               | 93    |
| Complications ( <i>n</i> )                                  |       |
| Port hernia   | 3/200 |
| Ileus   | 3/200 |
| Delayed bleeding  | 1/200 |
| DVT   | 1/200 |
| Potency after VIP using an EPIC quality of life instrument: |       |
| Any sexual activity (%):                                    |       |
| Men <60 years old:  |       |
| 3 months  | 65    |
| 6 months  | 82    |
| Men >60 years old:  |       |
| 3 months  | 50    |
| 6 months  | 75    |
| Sexual intercourse (%):                                     |       |
| Men <60 years old:  |       |
| 3 months  | 25    |
| 6 months  | 64    |
| Men >60 years:  |       |
| 3 months  | 10    |
| 6 months  | 38    |

BMI, body mass index; PSA, prostate-specific antigen; DVT, deep vein thrombosis. VIP, Vattikuti Institute Prostatectomy; EPIC, expanded prostate cancer index composite.

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## Brachytherapy of localized prostate cancer

Serdar Deger

Brachytherapy is defined as any local application using radioactive isotopes. About 1901, Pierre Curie was the first to have the vision of using a radioactive source for local treatment of malignancies. Paschkis, Pasteau, Degrais, and Denning were the pioneers between 1910 and 1922 who used radium in the urethra.<sup>1-3</sup> Barringer inserted radium needles into the prostate in 1915.<sup>4</sup> In the mid 1950s, lowenergy radioisotopes were developed. In 1952, Flocks injected colloidal gold into the prostate. In 1970, the Sloan Memorial Kettering Cancer Center (MSKCC) started to test iodine 125 for prostate cancer.

In the 1990s, technical changes made brachytherapy an attractive treatment alternative for lower tumor stages.

There are two defined brachytherapy categories: low dose rate (LDR) and high dose rate (HDR) brachytherapy. The two differ in dose rates of radioisotopes and treatment strategies. Common radioisotopes for LDR brachytherapy are iodine-125 ( $I^{125}$ ) and palladium-103 ( $Pd^{103}$ ), whereas gold-198 ( $Au^{198}$ ) and iridium-192 ( $Ir^{192}$ ) are radioisotopes for HDR treatment.

Table 44.1 shows the radiobiologic differences between these isotopes.

**Table 44.1** *Radiobiologic of commonly used radionuclides*

| Source           | Half-life (days) | Energy (keV) | Initial dose rate (cGy/h) |
|------------------|------------------|--------------|---------------------------|
| <i>Permanent</i> |                  |              |                           |
| $I^{125}$        | 60.2             | 28           | 5.8                       |
| $Pd^{103}$       | 17               | 21           | 15.3                      |
| $Au^{198}$       | 2.7              | 412          | 21.4–27                   |
| <i>Temporary</i> |                  |              |                           |
| $Ir^{192}$       | 74.2             | 380          | 60–90                     |

### Low dose rate brachytherapy

#### *Iodine-125 and palladium-103*

Iodine-125 was introduced in 1970 by Hilaris and Whitmore using an open retropubic approach (Figure 44.1). As a radioisotope with a long half-life of 60 days, which allowed



a continuous irradiation, at first it evoked euphoria.<sup>5,6</sup> Unfortunately, data between 1970 and 1980 clarified that iodine was not suitable for patients who had capsule invasive disease and/or undifferentiated cancer.



**Figure 44.1** An  $I^{125}$  seed. Reproduced with permission from *New perspective in prostate cancer*, 2nd edn., Belldegrun A, Kirby RS, Newling DWW, eds. Oxford: Isis Medical Media Ltd., 2000; 184, Figure 17.1.

Palladium-103 ( $Pd^{103}$ ) was introduced in 1987. Characteristics of  $Pd^{103}$  are similar to  $I^{125}$ . It emits a lowenergy photon with an average energy of 21 keV, and has a half-life of 17 days.<sup>7,8</sup> The first consideration was that tumors with an increased proliferative rate should respond better to  $Pd^{103}$  and tumors with low doubling rate should respond better to  $I^{125}$ . However, there have been no clinical trials to verify this consideration.<sup>9</sup>

In the early 1990s technical improvements, such as 3-D computer planning systems with online planning modalities and transrectal ultrasound (TRUS), led to an increase of LDR treatments in patients with prostate cancer.

The introduction of prostate-specific antigen (PSA) enabled prostate cancer to be diagnosed in the early stages, which allowed a better patient selection. Patients were separated in different risk groups (low-, intermediate-, and high-risk groups) and dose descriptions were adapted to those.

In 1995, the American Association of Physics and Medicine Task Group No. 43 (TG-43) recommended an algorithm for calculating the doses of  $I^{125}$  and  $Pd^{103}$ .<sup>10</sup> The American Brachytherapy Society (ABS) recommended adaptation of these doses for

Pd<sup>103</sup> and revised the dose of I<sup>125</sup> to unify LDR dosimetry. Patients with I<sup>125</sup> implants were to receive 144 Gy, and patients with Pd<sup>103</sup> implants were calculated to receive 115–120 Gy using the point source approximation.<sup>11–13</sup>

According to the ABS recommendations, candidates for an LDR monotherapy are stage T1–T2a, Gleason score 2–6, and PSA <10 ng/ml. Patients with clinical stage T2b–T2c or Gleason score 8–10 or PSA >20 ng/ml need an additional external radiotherapy. LDR was relatively contraindicated for patients with increased risk factors to develop complications, such as a high AUA (American Urological Association) symptom score, a large median lobe, history of multiple pelvic surgery, previous pelvic irradiation, technical difficulties which may result in inadequate dose coverage, severe diabetes with healing problems, previous transurethral resection of the prostate (TURP), gland size more than 60 ml at the time of implantation, and positive seminal vesicles.<sup>13</sup>

Between 1970 and 1985, 1013 patients with stage T2–T3 lesions were treated with pelvic lymph node resection and I<sup>125</sup> implantations at MSKCC. The approach consisted of an open exploration of the prostate.<sup>6</sup> All rectal and urinary complications resolved spontaneously.<sup>14</sup> The 15-year overall local disease-free survival was 60% in patients with stage T2 and T3 tumors and negative nodes who received a peripheral dose of 140 Gy or more.<sup>15</sup>

Kuban et al defined clinically progression-free survival as no evidence of disease (NED) (in the absence of PSA value).<sup>16</sup> Other study groups, e.g. Peschel et al and Rohloff et al, demonstrated similar results.<sup>17,18</sup>

Radge and Korb published data of 152 patients who were treated with I<sup>125</sup> implants: 98 patients with lowgrade/low-stage disease received monotherapy; 54 patients received an additional 45 Gy external radiation. The 10-year disease-free survival (PSA <0.5 ng/ml) was 60% for the group who received monotherapy and 76% for the combined therapy group.<sup>9</sup>

Beyer and Priestley reported on 489 T1–T2 patients in 1997, with median PSA of 7.3 ng/ml, treated with I<sup>125</sup> monotherapy.<sup>19</sup> The 4-year biochemical disease-free rate was 88% for patients with Gleason score ≤4, and 60% for those with Gleason score ≥5.

Blasko et al<sup>20</sup> published results of Pd<sup>103</sup> monotherapy (*N*=230 patients) with clinical stage T1–T2 tumors (56.1% of the patients had a T2a lesion, 28.3% a T1c lesion). The initial PSA level in 75.7% of the patients was <10 ng/ml, 40% of the patients had a Gleason score ≥7, and the overall biochemical control rate at 9-year followup was 83.5% of patients. Failures were local in 3.0%, distant in 6.1%, and PSA progression was observed in 4.3% of patients. Failure was defined as a PSA progression of two consecutive rises in serum PSA. This was different from the ASTRO (American Society of Therapeutic Radiology and Oncology) Consensus Conference definition,<sup>21</sup> which required three rises as definition for failure.

In 2000, Beyer and Brochman published data of 1527 and 695 patients with T1 or T2 Nx–N0M0 prostate cancer treated between December 1988 and December 1995 with either external beam radiation therapy (EBRT) or brachytherapy (BT), respectively. EBRT and BT appeared to be equally efficacious for low-risk patients with T1/T2 tumors and Gleason scores 6 and PSA <10 ng/dl at 5 years. Patients with Gleason scores 8–10 or PSA between 10 and 20 ng/dl appeared to fare worse with BT alone compared with EBRT. Neither EBRT nor BT were particularly effective for patients presenting with a PSA over 20 ng/dl.<sup>22</sup>

Critz et al combined EBRT with LDR treatment for the early stages of prostate cancer. They reported on about 689 patients treated between 1992 and 1996. Disease-free status was defined as the achievement and maintenance of a PSA nadir of 0.2 ng/ml or less. Median follow-up was 4 years (range 3–7 years). None of these men received neoadjuvant or adjuvant hormonal therapy. Overall 5-year disease-free survival was 88%. Multivariate analysis revealed that pretreatment PSA was the strongest indicator of subsequent disease-free status in regard to Gleason score or clinical stage.<sup>23</sup>

Dattoli et al treated 124 patients with unfavorable risk factors, such as T3 tumor, Gleason score >6, PSA >15 ng/ml, with Pd<sup>103</sup> plus external irradiation of 41 Gy. Biochemical progression-free survival was 79% at 3-year follow-up; potency protection was 77%.<sup>24</sup>

Looking at the literature, there are several studies published in regards to LDR brachytherapy, with different definitions of patient risk and biochemical failure. Mostly, patients with a PSA <10 ng/ml, Gleason score <7, and stage ≤T2a were defined as low-risk patients. For these patients, biochemical control was between 50 and 100%. Biochemical failure was defined as a PSA between 0.5 and 1 or, in some series, >4 ng/ml, or a two-time continuous rise.<sup>19,25–29</sup> In moderate-risk patients, defined as those with a PSA value between 10 and 20 ng/ml, biochemical survival ranged from 45% to 82%.<sup>19,20,28–32</sup> In high-risk patients, characterized by a PSA >20 ng/ml or a Gleason score >7, the 5-year biochemical control rates of 30–65% proved unsatisfactory.<sup>19,20,29–32</sup>

Combining EBRT with implants improved the 10-year biochemical survival from 64 to 76% (PSA failure definition was PSA >0.5 ng/ml).<sup>26,33</sup>

The main interest of patients asking for LDR brachytherapy is preservation of potency. Stock et al showed clearly the dosage dependence of sexual potency preservation. Erectile function was assessed using the scoring system of:

- 0—complete inability to have erections,
- 1—able to have erections but insufficient for intercourse,
- 2—can have erections sufficient for intercourse but considered suboptimal and
- 3—normal erectile function.

In 313 patients with potency score 2 or greater before therapy the no decrease in erectile function score was experienced by 64% and by 30% at 3- and 6-year follow-up. The preservation of potency was 79% and 59% at 3 and 6 years, respectively. Two factors had a significant negative effect on potency in univariate and multivariate analyses. These were high implant dose (D90>160 Gy for I<sup>125</sup> and D90>100 Gy for Pd<sup>103</sup>) and a pretreatment erectile dysfunction. The rate of potency preservation after brachytherapy was high, but decreased from 3 and 6 years after treatment.<sup>34</sup>

In combination with EBRT, the sexual potency rate dropped in different groups.<sup>27,35,36</sup>

Potters et al reported that potency was preserved in 311 of 482 patients, with a 5-year actuarial potency rate of 52.7%. The 5-year actuarial potency rate for patients treated with LDR-brachytherapy as monotherapy was 76%, and for those treated with additional EBRT was 56%. Patients treated with neoadjuvant androgen deprivation (NAAD) had a 5-year potency rate of 52%, whereas those with combination EBRT+LDR brachytherapy+NAAD had a potency rate of 29%. Of 84 patients treated with sildenafil, 52 (62%) had a response.<sup>36</sup>

Rectal complications were rare but grade 3–4 complications (e.g. rectal ulceration, bowel obstruction, fistula formation, proctitis requiring blood transfusion, etc.) were seen. Radiation proctitis following LDR brachytherapy alone occurred in 1–5%.<sup>19,32</sup> Adding EBRT, the rate increases to 7–21%, mostly grade 2–3 complications. Rectal fistula occurred in 1–2.4%.<sup>29,37–39</sup>

It is difficult to analyze the data for each isotope, due to the absence of prospective randomized trials. The benefit of neoadjuvant-adjuvant hormonal treatment and/or additional EBRT is not documented; data indicate no difference in outcome between I<sup>125</sup> and Pd<sup>103</sup>.<sup>29,31,40</sup>

### High dose rate brachytherapy

#### *Gold-198*

In 1952, Flocks et al introduced gold-198 for the treatment of prostate cancer. Because of a half-life of 2.7 days and penetration depth of 3 mm, gold-198 was ideal for an operative field. In T3 disease, Flocks et al injected 100 mCi of colloidal gold-198 after radical prostatectomy into the pedicles.<sup>41</sup> Complication rate in these patients ( $n=345$ ) was low; 4.4% of patients had local progression of disease. Progression-free survival in patients with no lymphatic involvement was 74% after 5 years, 66.7% after 10 years, and 27.5% after 15 years treatment.<sup>42</sup>

Colloidal gold-198 was not available after the mid 1970s. Then, gold seeds were implanted into the pedicles after radical prostatectomy. Between 1977 and 1988, 80 patients were treated with this adjuvant radiation therapy (73.8% of them had T3 disease). Ten-year progression-free survival was 84.4% for pT2 tumors and 79.1% for pT3 tumors.<sup>43</sup> In 1997, Loening published long-term follow-up data of patients who were treated with gold seed implantation as primary therapy between 1984 and 1995. The median follow-up was 4 years, and cancer-specific survival was 100% for T1 and T2a, 90% for T2b, and 76% for T3 tumors. The negative biopsy rate 5 years after treatment was 80%. The overall complication rate was low; however, 2 patients developed rectal ulceration, with 1 requiring a colostomy.<sup>44</sup>

Butler et al reported in 1997 the Baylor College experience based on 510 patients, treated between 1965 and 1980. Gold-198 was implanted as boost to an additional EBRT. The implantation was performed by an open retropubic approach. Mean total dose was 69 Gy (45–105 Gy). In this study 23% of the patients had T3 tumor and 30% of patients had lymphatic metastases. Survival rates for all stages were  $83\pm3\%$  after 5 years,  $53\pm5\%$  after 10 years, and  $25\pm10\%$  after 15 years.<sup>45</sup>

The Baylor College group treated 54 patients between 1992 and 1996; 40.7% of these patients had a T1, 50% had a T2 and only 7.4% of them had a T3 lesion. The total dose delivered averaged 71 Gy (59–85 Gy). Additional EBRT was given in 9 patients only. Single acute toxicity was reported in 22 patients and multiple acute toxicity in 20 patients. Toxicity according to the RTOG (Radiation Therapy Oncology Group) toxicity criteria included proctitis in 50.9%, urethritis in 39.5%, and cystitis in 37.7% of patients. Late rectal toxicity occurred in 6.3% and radiation cystitis occurred in 16.7%. No grade III or IV acute or late toxicity was seen. Eighty-one percent of patients with an initial

PSA level >4–10 ng/ml reached a PSA nadir of less than 1 ng/ml, while only 65% with an initial PSA level >10 ng/ml achieved a PSA nadir <1 ng/ml. Median follow-up was between 12.5 to 21.6 months.<sup>45</sup> Table 44.2 summarizes progression-free survival data using gold-198.

### *Iridium-192*

The activity of iridium-192 is 16 times higher than that of cobalt-60. The half-life of iridium-192 is 74.4 days. Delivered electron energy is between 0.097 and 0.67 MeV. Because of the low gamma energy, radioprotection is much better than with radium: 5 cm lead or 2.6 cm uranium provide enough effective protection.<sup>48</sup> Iridium is used primarily for temporary implant because of its high dose performance. It is used as an LDR and also as an HDR technique.<sup>49,50</sup>

Iridium-192 in an LDR technique has been used since 1977.<sup>51</sup> Tumor control rates of 90–95% were demonstrated, using clinical criteria for failure with follow-up from 1 month to 60 months.<sup>52–60</sup> Because PSA levels are lacking in these studies, the data are currently not useful.

Syed et al published their results on 200 patients who were treated between 1977 and 1985. The open surgical approach was used for placing iridium-192. In addition, 30–40 Gy of external irradiation were given. Local tumor control rates were between 90 and 95.5% and 4–11% of patients had complications such as proctitis and urethral strictures. A significant correlation was found between complications and previously performed TURP. One patient required a colostomy.<sup>61</sup>

In 1986, Porter et al described a transperineal open surgical application with a device called the MicroSelectron. The MicroSelectron had a plastic ribbon connected to a storage container. Ribbons were fed into a control channel, where they were moved remotely and cut to the desired length. The ribbons were attached to leaders, which were coupled to the MicroSelectron drive system. The system was attached to a patient through a coupling adapter under continuous monitoring.<sup>59</sup> The era of the afterloading technique began with the MicroSelectron system. The advantage of this system is the safety to radiation exposure. Khan et al reported results in 321 patients. The delivered interstitial dose was 3100 cGy to a total dose of 6500 cGy. According to the RTOG system, grade II complications, such as mild dysuria, diarrhea, and proctitis were observed in 0.6–6.5% of the patients, whereas grade III complications were seen in 3 patients. The 5-year local tumor control was 95% for T1c, 93% for T2a, 83.6% for T2b, and 73.1% for T3 tumors.<sup>62</sup>

The establishment of the afterloading technique, based on a treatment plan adapted to the actual geometry of the prostate using computer algorithms to allow a more homogeneous dose within the implant for better tumor coverage, were milestones of modern HDR brachytherapy.

The aim of HDR brachytherapy is to deliver the maximal radiation dose into the prostate while minimizing the radiation dose to the surrounding tissue. Hsu et al published the critical volume tolerance analysis to estimate the potential for further dose escalation using HDR brachytherapy as boost. Dose-volume histograms were plotted for comparison of 7 field conformal EBRT and HDR brachytherapy techniques. Dosage to the normal structures was calculated. The HDR delivered higher doses into the prostate and less to the bladder and rectum.<sup>63</sup>

Different study groups have used HDR brachytherapy in the treatment of localized prostate cancer since the mid 1990s.<sup>64–69</sup> Most data were published by four study groups: the Charité Hospital in Berlin, Germany;<sup>70</sup> the Christian Albert University in Kiel, Germany;<sup>71</sup> the Göteborg-Sahlgrenzka University Hospital in Göteborg, Sweden;<sup>67</sup>

**Table 44.2** *The 5- and 10-year progression-free survival using gold-198*

| Main author             | Progression free survival (%) |       |       | Follow-up (years) |
|-------------------------|-------------------------------|-------|-------|-------------------|
|                         | T1                            | T2    | T3    |                   |
| Loening <sup>44</sup>   | 100                           | 90    | 76    | 5                 |
| Butler <sup>45</sup>    | 76±12                         | T2a   | T2b   | 10                |
|                         |                               | 61±12 | 53±16 |                   |
| Carey <sup>46</sup>     |                               | 60    | 63    | 7                 |
| Gutierrez <sup>47</sup> |                               | 85    | 43    | 10                |
| Lannon <sup>49</sup>    | 83                            | T2a   | T2b   | 10                |
|                         |                               | 91.3  | 64.4  |                   |

and the William Beaumont Hospital (WBH) in Royal Oak, Michigan.<sup>72</sup> Interstitial doses were between 8.25 and 15 Gy in all institutions. Follow-up was between 30 and 98 months. Tumor stages were almost identical, with T3 disease between 13 to 32%. The percentage of T3 disease of the Charité group was 58%: the Charité group performed laparoscopic staging lymph node dissection in all patients. The Sahlgrenzka University Hospital group did a staging lymphadenectomy in only 20 patients. Patients of the William Beaumont Hospital and Christian Albert University had no surgical lymph node staging. Five-year biochemical survival (according to ASTRO criteria<sup>21</sup> with three times rising PSA value, except at Sahlgrenzka University Hospital) as shown in Table 44.3, and ranged from 67% to 84%.

Late grade 2–3 (RTOG) rectal complications were seen in 11% and grade 2–3 urinary complications in 6% of the patients at the Christian Albert University.<sup>71</sup> Late grade 3–4 complications at the Charité occurred in 12.2%, urethral strictures occurred in 7.4%, and 3% of patients suffered from grade 2–3 incontinence; 4 patients developed a rectourethral fistula after rectal ulceration requiring a colostomy. Therefore, the interstitial radiation dose at the Charité was reduced after December 1993 from 10 Gy to 9 Gy per session.<sup>70</sup>

HDR brachytherapy has also been used as monotherapy. In this technique, the template was fixed to the perineum and fractioned interstitial doses of 6 Gy were delivered. The total dose was 48–54 Gy.<sup>73</sup>

### Low dose rate technique

Since the introduction of LDR brachytherapy, seed placement was performed with the guidance of a preplanned implantation technique. The preplanned method had a number of disadvantages such as patient positioning and setup, and images taken during the actual implant procedure had to be matched with those obtained during the preimplant planning study. The latter was occasionally difficult to reproduce in the operating room (OR). Alterations in the prostate volume and shape occurred during the interval between

preplanning and implantation because of changes in patient position and relaxation of pelvic musculature induced by anesthesia or as a result of hormonal therapy. These changes had caused inaccuracies in an implant based solely on the preplanned images. The preplanning requires a separate TRUS imaging study, which is cumbersome and sometimes difficult to schedule. Furthermore, a separate pubic arch obstruction evaluation study is required in some preplanning techniques.<sup>74</sup>

The ABS reported in 2001 that the preplanned technique for permanent prostate brachytherapy had limitations that could be overcome by an intraoperative planning. They proposed the following terminology in regard to the prostate planning process, with five levels of prostate brachytherapy:

1. Preplanning—creation of an operative plan a few days or weeks before the implant procedure.
2. Intraoperative preplanning—creation of a plan in the OR just before the implant procedure, with immediate execution of the plan.
3. Intraoperative planning (treatment planning in the OR)—the patient and transrectal ultrasound probe are not moved between the volume study and the seed insertion procedure.
4. Interactive planning—stepwise refinement of the treatment plan using computerized dose calculations derived from image-based needle position feedback.
5. Dynamic dose calculation—constant updating of dose distribution using continuous deposited seed position feedback.

The elements of an intraoperative planning system should include the following steps:

- treatment planning in the OR
- image acquisition
- target definition
- organ segmentation (draw contours manually)

**Table 44.3** *Patient characteristics of high dose rate groups*

| Study                         | No. | Age<br>(years) | Initial median<br>PSA(ng/ml) | Single<br>interstitial<br>dose (Gy) | External<br>dose (Gy) | Follow-up<br>(months) | 5-year<br>PFS <sup>a</sup><br>(%) |
|-------------------------------|-----|----------------|------------------------------|-------------------------------------|-----------------------|-----------------------|-----------------------------------|
| Michigan/USA <sup>72</sup>    | 161 | 69             | 9.9                          | 8.25–10.5                           | 46                    | 30                    | 67                                |
| Göteborg/Sweden <sup>67</sup> | 50  | 63             | –                            | 10                                  | 50                    | 45                    | 84 <sup>b</sup>                   |
| Kiel/Germany <sup>71</sup>    | 144 | 68             | 12.15                        | 9                                   | 50                    | 98.4                  | 77.2                              |
| Charité/Germany <sup>70</sup> | 230 | 67             | 12.8                         | 9–10                                | 45–50.4               | 40.2                  | 69                                |

<sup>a</sup> Progression-free survival.

<sup>b</sup> Prostate-specific antigen (PSA) 1 ng/ml.

- identification of needle position in relation to prostate
- intraoperative optimization based on imaged needle location
- estimation of seed positions from imaged needle position
- updating of dose calculation based on imaged needle location
- auto organ segmentation

- capturing deposited seed positions in real time
- optimization based on deposited seed location
- dynamic updating of dose calculation based on actual seed position
- account for motion of prostate during placement
- account for intraoperative edema
- postimplant dose calculation at time of surgery
- account for postoperative edema.

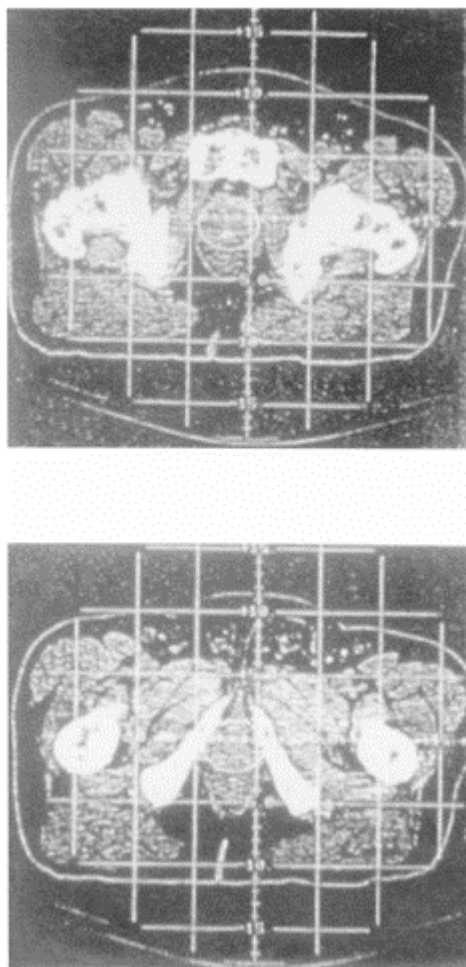
Intraoperative preplanning eliminates the preplanning patient visit. Therefore, the approximate number of seeds to be ordered has to be determined from a nomogram or table based on the prostate volume obtained from a computed tomography (CT) scan or an ultrasound (Figure 44.2). TRUS is performed in the OR, and the images are imported in real time into the treatment planning system (Figure 44.3). The target volume, rectum, and urethra are contoured on the treatment planning system either manually or automatically, and a treatment plan is generated. The seeds are implanted into the prostate according to the plan.

Intraoperative preplanning makes two separate TRUS procedures as required in the two-step preplanned method as well as reproducing patient positioning, and setup unnecessary. However, intraoperative preplanning does not account for intraoperative changes in prostate geometry or deviations of needle position from the preplan.<sup>75</sup>

An optimized treatment plan is then performed, the dose-volume histogram (DVH) is generated, and the plan is examined. Seeds can be added or deleted manually, and the new isodose distributions and DVH displays are regenerated if necessary (Figure 44.4). The needles can now be inserted as per plan. In interactive planning, it is critical that the dose calculation is updated based on estimated seed positions derived from actual needle positions. The needles need to be repositioned, or needle positions can be changed in the plan if there are adverse dosimetric consequences. The dose calculation is then updated, based on the actual needle location. The interval at which the dose distribution is recalculated is operator-dependent.

Various interactive planning systems exist: some are commercially available, whereas others are institutionbased systems.<sup>74</sup> Commercially available systems include the Interplant system (Burdette Medical System, Champaign, Illinois), PIPER (RTek, Pittsford, New York), SPOT (Nucletron Corporation, Veenendaal, The Netherlands), Strata (Rosses Medical Systems, Columbia,





**Figure 44.2** Pretreatment CT scans with the traced prostate. Note the relationship between the prostate and pubic arches. Reproduced with permission from New perspective in prostate cancer, 2nd edn., Belldgrun A, Kirby RS, Newling DWW, eds. Oxford: Isis Medical Media Ltd., 2000; 187, Figure 17.2.

Maryland), and VariSeed (Varian Medical Systems, Palo Alto, California). The institution-based systems include those at the MSKCC and Brigham and Women's Hospital in Boston.

In the technique of Stock and Stone et al<sup>76-79</sup> the implantation begins with the insertion of needles, 1 cm apart, into

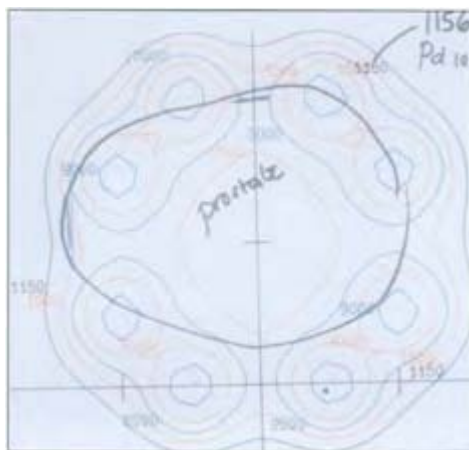


**Figure 44.3** Intraoperative transrectal ultrasound images with grid overlay. Reproduced with permission from *New perspective in prostate cancer*, 2nd edn., Belldegrun A, Kirby RS, Newling DWW, eds. Oxford: Isis Medical Media Ltd., 2000; 188, Figure 17.3.

the periphery of the gland at the level of the largest TRUS transverse diameter cut as a guide. The position of the needles is determined on the TRUS images by identifying the echo bright markings, the so-called 'acroflash', of the implanted needles. Seventy-five percent of the seeds are then implanted through these peripheral needles using a Mick applicator. The seed positions are marked on the planning system along the needle track, and isodoses are generated. The remaining 25% of the seeds are implanted using about 6–8 needles in the prostate interior such that they remain 0.5–1 cm from the urethra and cover the periphery of the base and apex. The needle positions in the interior are optimized to limit dose action on normal structures (urethra and rectum) and minimize cold or hot areas within the prostate.

The MSKCC technique<sup>80,81</sup> relies on an inverse planning optimization program, which uses a genetic algorithm optimization system,<sup>82-85</sup> that attempts to find seed positions on a grid of available or potentially available points. It sites that satisfy the dose constraints for the normal organs, such as the urethra and rectum, while maintaining maximal target

coverage with the prescription dose to the prostate. This interactive optimization process analyzes more than 106 possible seed locations to achieve the ideal fit and solution and requires approximately 5–10 min for completion in the operating program. The computer determines the ideal seed location that meets the predetermined dose constraints for the urethra and rectum, and



**Figure 44.4** A dose-volume histogram of the prostatic apex. The dose drops in the center of the gland. Reproduced with permission from New perspective in prostate cancer, 2nd edn., Belldegrun A, Kirby RS, Newling DWW, eds. Oxford: Isis Medical Media Ltd., 2000; 188, Figure 17.4.

the target dose. The seeds are loaded using a Mick applicator according to the seed-loading pattern dictated by the plan.

Lo, et al<sup>86</sup> compared the dosimetry results intraoperatively to CT-based evaluation performed 1-month postimplant. They reported a good correlation between intraoperative and postimplant results using intraoperative planning. The mean D90 results intraoperatively compared to those seen postimplant were 178 Gy vs 188.5 Gy for iodine-125 implants and 98 Gy vs 98.5 Gy for boost palladium-103 implants, respectively.

Zelevsky et al demonstrated excellent dose coverage of the prostate with the use of interactive planning.<sup>80</sup> They also showed in a comparative dosimetric analysis of three implant techniques used at MSKCC that lower maximal urethral doses were observed significantly more frequently with the intraoperative computer-generated conformal plan in comparison to a CT preplan approach or an intraoperative ultrasound manually optimized approach.<sup>80,81</sup> Postimplant dosimetric analysis is standard practice following temporary brachytherapy procedures. Its role following permanent implants is less well

established. Previous surveys have shown wide variation in dosimetric methods.<sup>87,88</sup> The ABS organized a panel to develop guidelines for the performance and analysis of postimplant dosimetry.<sup>89</sup> Because the treatment plan and the actual implantation are completed at the time of postimplant analysis, the rationale for its use needs elucidation. The first issue arises from the fact that brachytherapy is an imperfect modality and, certainly, the permanent ultrasound-guided prostate implant technique is no exception. The dose distributions following implantation are not the same as those planned prior to the implant.<sup>90-95</sup> Consequently, it is important to document the actual dose that the prostate and normal adjacent tissues will receive over the life of the implant for evaluating the outcome. Significant underdosing can lead to treatment failure. In this case, additional seed implantation or supplementary EBRT is necessary to achieve the dose.<sup>96</sup> CT-based evaluation of the prostate implant appears to best satisfy the requirements of seed localization target and normal structure delineation and seed-target registration. Because of the possibility of seed migration, the number of implanted seeds may not be the same as the number of seeds present in the prostate at the time of the postimplant CT scan. Therefore, a better approximation of the number of seeds may be obtained by using plane radiographs. The CT technique recommended by the ABS should include the prostate, all the seeds within and around the prostate, and any critical structures for which the dose is to be reported. To accomplish this, it is suggested that a minimum of 2-cm margin be added to the superior and inferior extent of the prostate. A reduced field of view that completely encompasses the volumes and structures of interest, but offers a finer resolution in the plane of the implant, should be used. This reduces the error associated with seed localization and prostate boundary definition. Contiguous axial slices are recommended to reduce the chance of missing seeds between scans. The slice thickness and spacing should not be greater than 5 mm. A catheter placed in the bladder and filled with contrast medium serves to localize the urethra and internal bladder wall. The geometry of the implant, and therefore the dosimetry, is derived directly from the CT images themselves. In some CT scans, the images may contain distortions (such as unequal x and y scaling), and it is important that means of identifying and accounting for such scaling variations be in place.

The TG-43 formalism is recommended for both the preand postimplant dosimetry.<sup>98-</sup>

<sup>101</sup> Calculations should be performed using a matrix with resolution limited to 2 mm or less<sup>102</sup> in an effort to minimize the effects of the large dose gradients inherent in a brachytherapy procedure. Normal structures of interest that can be defined by using CT include the urethra and the rectum. The entire prostatic urethra should be defined. Of the rectum only the anterior rectal wall is considered to be a structure of interest.

The values of D100, D90, and D80 represent the doses that cover 100%, 90%, and 80% of the prostate, respectively. The values of V200, V150, V100, V90, and V80 stand for the fractional volume of the prostate that receives 200%, 150%, 100%, 90%, and 80% of the prescribed dose, respectively. The total volume of the prostate (in ml) is obtained from postimplant dosimetry. The number of days between implantation and the date of the imaging study is used for dosimetric reconstruction. The urethral and rectal doses have to be reported to allow adequate evaluation of postimplant dosimetry and to allow correlation with clinical outcome according to ABS recommendations.

## Summary

In summary, brachytherapy for prostate cancer is an alternative treatment. Patient selection is important for choosing the accurate technique. LDR monotherapy seems to be appropriate for patients with low-risk disease (T1–T2a tumor, PSA <10 ng/ml, and Gleason score <7).

Looking at advanced disease, dose escalation seems to be necessary. There is no doubt that patients receiving radiation doses exceeding 72 Gy had significantly better biochemical and clinical disease-free survival rates.<sup>103</sup> Advanced disease may benefit from dose escalation with or without synergistic treatment combinations such as interstitial hyperthermia or neoadjuvant-adjuvant antiandrogen therapy.<sup>104–107</sup>

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## High-intensity focused ultrasound for the treatment of prostate cancer: the European experience

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### Introduction

Since 1989, high-intensity focused ultrasound (HIFU) has been utilized to treat prostate cancer. Preclinical in-vitro and in-vivo studies have established that cancerous tissues may be destroyed with HIFU through coagulative necrosis,<sup>1-3</sup> without cell spread.<sup>4</sup>

The transrectal approach for HIFU administration was validated on a canine model.<sup>5</sup>

In 1992, the first human HIFU study was used to treat benign prostatic hyperplasia (BPH). With the study, the feasibility of the transrectal HIFU for the destruction of prostate tissue was successfully demonstrated.<sup>6</sup> The clinical development of HIFU for prostate cancer has been carried out from 1993 to the present. An overview of the results observed with the Ablatherm prototypes and the standard device is provided in the following sections.

### Materials and methods

#### *Clinical studies*

During the clinical development, the feasibility to target and to treat the prostate, the histology of the HIFU lesion, and the clinical outcomes were assessed in several different clinical trials.

The Pilot Studies I and II (1993–95), monocentric clinical trials with the first device prototype, were performed in patients with prostate cancer, and  $n=15$  and  $n=11$  patients were included, respectively.<sup>7</sup> These investigations confirmed that it was possible to target the prostate and to destroy cancerous cells. In addition, this preliminary study led to the implementation of several device safety features, which are discussed in a later section.

The European Multicentric Study<sup>8</sup> (1995–2000 for the completion of the patient recruitment) is being conducted in six investigational sites, with a total of  $n=652$  prostate cancer patients being treated. Outcomes are being assessed for HIFU treatment safety and efficacy. This clinical study is still ongoing for the long-term assessment of outcomes.

In parallel, the Nijmegen Study (1997–98) evaluated the histology finding after partial HIFU treatment of the gland in 17 patients who subsequently underwent a radical prostatectomy within 2 weeks of transrectal HIFU therapy.<sup>9–11</sup>

All these clinical investigations are prospective, openlabeled, single-arm clinical trials. They were performed in accordance with the Declaration of Helsinki, the European Standard EN 540, and the local regulations for clinical trials. The studies were approved by local Ethics Committees, and all the patients signed an informed consent form prior to their enrollment.

### *Devices*

All the patients were treated using the Ablatherm device (EDAP S.A., Lyon, France).

### **Components**

The components of the HIFU device are described below:

- an *endorectal probe* composed of two ultrasonic transducers—a high-energy therapy transducer and an imaging transducer
- an *ultrasound scanner* connected to the endorectal probe enables imaging of the target tissue on a monitor
- a *treatment module*, consisting of a patient treatment table, a motorized endorectal probe positioning unit, a high-frequency generator to power the transducer, and a computer to control device operation and builtin safety features.

From the initial HIFU prototype (Figure 45.1) to the current HIFU model, CE mark (January 2000), (Figure 45.2), safety devices have evolved.

### **Safety features**

As a result of the first clinical investigation, safety features were progressively added to protect the patient and improve treatment application. These features are described below:

- *A-mode scanning*: to continuously monitor the distance between the transducer and the rectal wall in order to ensure the proper distance is maintained in order to prevent injury to the rectum. The software blocks active firing in the event of unsafe distances between the transducer and rectal wall.
- *Safety ring*: installing a safety ring around the therapy transducer makes it possible to maintain the constant position of the probe, in relation to the rectal wall, as it rotates between the imaging and treatment modes.
- *Software to identify rectal wall*: this specialized software is used to assist the operator by identifying the position of the rectal wall and automatically aligning the targeted lesions 3–6 mm ahead of it. The software also limits the rotational movements of the treatment head, which, if excessive, could cause the rectum to move away from the therapy transducer.

- *Anticavitation coupling liquid*: a degassed, anticavitation liquid is used as a coupling liquid to prevent any bubbles from forming in the path of the ultrasound (which could interfere with rectal distance measurement).



**Figure 45.1** First device prototype (1992). (Courtesy of EDAP S.A., Lyon, France.)



**Figure 45.2** Standard device (CE mark). (Courtesy of EDAP S.A., Lyon, France.)

- *Cooling system*: continuously circulates cooling fluid to protect the superficial rectal mucosa from thermal injury.
- *Patient movement alarm*: an audible alarm warns the operator in the event of inadvertent significant patient movement during treatment, and automatically stops HIFU firing.

The primary goal of the above safety features is to preserve surrounding tissues, i.e. the protection of the rectal wall as the posterior part of the prostate is treated.

### Technical parameters

Technical parameters evolved in parallel with safety features in order to improve the HIFU performance in treating localized prostate cancer. The HIFU frequency progressively increased from 2.25 MHz to 3.0 MHz, while the shot duration lengthened from 4 to 5 s, and 4.5 s for retreatments (i.e. after previous HIFU, previous external beam radiation therapy, or previous radical surgery). In all cases, a 5 s time interval is maintained between HIFU firings.

The energy is delivered via an endorectal probe, which includes both the imaging (Figure 45.3) and the firing transducer (Figure 45.4). The high-energy ultrasound waves propagate through the rectal wall (Figure 45.5) and are focused on the prostate, generating intense heat and causing the ablation of prostate tissue within the focal area.



**Figure 45.3** Transrectal probe—imaging mode. (Courtesy of EDAP S.A., Lyon, France.)

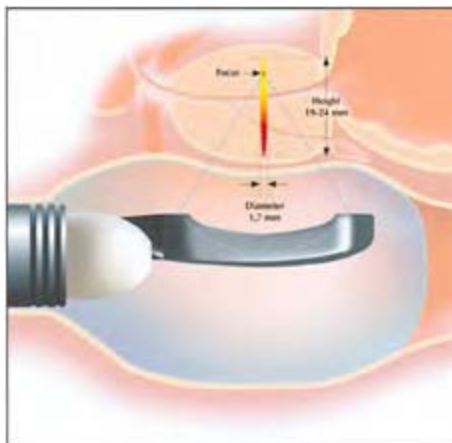


**Figure 45.4** Transrectal probe—firing mode. (Courtesy of EDAP S.A., Lyon, France.)

Each firing creates a large and reproducible lesion, which spans from the anterior to the posterior prostate capsule. The transducer movements allow for accurate positioning of the focal point and for defining the appropriate lesion depth (dynamic focusing) to match the prostate shape. Continuous firings are delivered repeatedly (Figure 45.6) to obtain a complete treatment of the whole gland while preserving the rectal wall and the surrounding tissues.

*Clinical procedure*

From 1993 to 1997, patients were systematically treated in two sessions, i.e. one session per lobe. The time interval



**Figure 45.5** HIFU principle. (Courtesy of EDAP SA, Lyon, France.)



**Figure 45.6** Firing sequence for the treatment of the targeted volume. (Courtesy of EDAP S.A., Lyon, France.)

between these two sessions was 1–3 months. However, since 1998, the HIFU treatment of both prostatic lobes has been performed in a single session.

During the follow-up, HIFU retreatments were performed on individuals with residual or recurrent intraprostatic tumors as documented by follow-up prostatic biopsies.

In order to preserve the external sphincter, an adequate safety margin for the (apex) treatment of the apical region was also further defined. Below this safety margin, the

portion of the apical prostate not directly targeted receives treatment via heat diffusion from adjacently treated tissue.

### **Standard procedure**

The standard procedure is now defined, and generally aims at treating the entire prostate gland in one 2–3 hour treatment session, although, if needed, a second treatment session can be performed at a minimum interval of 6 months after the first treatment session. The treatment is usually performed under spinal anesthesia. The patient is positioned on the treatment module and the endorectal probe is inserted. Ultrasound imaging is used to detect the contours of the prostate and the targeted treatment volume is defined on the computer screen. Under computer control, the device positions and successively repositions the treatment transducer and delivers HIFU energy according to consecutive treatment blocks defined by the user until all sectors of the prostate have been treated.

### **Efficacy results**

#### *Histologic results: the Nijmegen Study*

In this study, to confirm the histologic efficiency of HIFU, 17 patients scheduled for radical prostatectomy for localized prostate cancer underwent a partial treatment (one lobe in which the carcinoma was located) an average of 8 days (range 4–12 days) prior to surgery.<sup>9–11</sup> The excised prostatectomy specimen was then evaluated histopathologically to evaluate the effects of the treatment. Pathologic evaluation revealed that HIFU effects could be accurately recognized macroscopically as a dark red discoloration, with an abrupt transition to pink-white colored, nontreated tissue. This discoloration correlated very well with the coagulative and hemorrhagic necrosis seen on microscopy, with a sharp delineation between treated and nontreated tissue.

In 5 patients, viable tumor was found in the dorsal part of the prostate, and in 11 cases, viable tumor was present in the ventral part of the prostate, out of reach of the HIFU energy. In no patients was a viable tumor present in the treated area. In most cases, the carcinoma was still visible but not viable. In 3 cases out of 9 where biopsies of the pelvic floor were taken, clear-cut necrosis was seen, the other 6 showing only undisturbed muscular tissue. This indicated that, in some cases, the HIFU effect could extend a few millimeters beyond the targeted area.

This study also demonstrated that radical prostatectomy could be performed soon after HIFU treatment, although potentially there might be an increased risk of stenosis or stress incontinence. During the post-HIFU prostatectomy procedures, the periprostatic tissue appeared edematous but did not cause any serious intraoperative problems.

Following these study results, the treatment duration was increased to 5 s, in order to lengthen the lesion in the posterior part of the prostate where tumors are probably located.



*European Multicentric Study*

This clinical study started in November 1995, and involved six investigational sites. Patient recruitment was completed in October 2000, with  $n=652$  patients entered and treated. Patient follow-up is still ongoing.

An interim analysis was performed on all the patients included and treated up to November 1999. In total,  $n=559$  patients were analyzed, 402 of them being treated as primary treatment for localized prostate cancer.<sup>8</sup>

For the localized prostate cancer population ( $n=402$ ), patient baseline characteristics were (mean $\pm$ SD): age 69.3 $\pm$ 7.1 years, prostate volume 28.0 $\pm$ 12.7 ml, prostatespecific antigen (PSA) 10.9 $\pm$ 8.7 ng/ml (Table 45.1). Patient distribution according to the disease-related risk level is presented in Table 45.2, using the following definitions:

- low-risk patients: T1–T2a and PSA  $\leq 10$  ng/ml and Gleason score  $\leq 6$
- intermediate-risk patients: T2b or PSA  $\leq 20$  ng/ml or Gleason score = 7
- high-risk patients: T2c or PSA  $> 20$  ng/ml or Gleason score  $\geq 8$ .

At the time of the data analysis, the mean follow-up was 407 days (range 0–1541, Q1 135 days, median 321 days, Q3 598 days). For the biopsy assessment purpose, any positive core in biopsies performed after the last treatment session led to a ‘positive biopsy’ classification of the patient.

According to the above definitions, the observed negative biopsy rate was 87.2% in the localized prostate cancer population. When stratified according to the risk level, the negative biopsy rates were 92.1% in the low-risk subgroup, 86.4% in the intermediate-risk subgroup, and 82.1% in the high-risk subgroup.

**Table 45.1** *Patient baseline characteristics (European Multicentric Study)*

|                 | Age (years) | Prostate volume (ml) | PSA (ng/ml) | Gleason score |
|-----------------|-------------|----------------------|-------------|---------------|
| <b><i>n</i></b> | <b>396</b>  | <b>389</b>           | <b>397</b>  | <b>369</b>    |
| <b>Mean</b>     | <b>69.3</b> | <b>28.0</b>          | <b>10.9</b> | <b>6.0</b>    |
| SD              | 7.1         | 12.7                 | 8.7         | 1.3           |
| Q1              | 65.0        | 19.0                 | 5.8         | 5.0           |
| <b>Median</b>   | <b>70.0</b> | <b>25.0</b>          | <b>8.9</b>  | <b>6.0</b>    |
| Q3              | 75.0        | 34.0                 | 41.0        | 7.0           |
| Minimum         | 51.0        | 4.2                  | 0.1         | 2.0           |
| Maximum         | 88.0        | 120.0                | 78.0        | 9.0           |

PSA, prostate-specific antigen.

**Table 45.2** *Patient distribution according to the disease-related risk level (European Multicentric Study)*

| Risk level        | <i>n</i> | Percent |
|-------------------|----------|---------|
| Low risk          | 114      | 28.4    |
| Intermediate risk | 193      | 48.0    |

|           |     |       |
|-----------|-----|-------|
| High risk | 95  | 23.6  |
| Total     | 402 | 100.0 |

Biochemical relapse rate is not presented here. Indeed, most of the patients were enrolled in 1998–99, and at least 1 year of follow-up is needed for a first assessment of PSA stability according to the American Society of Therapeutic Radiology and Oncology (ASTRO) definition (time to nadir+at least 3 successive PSA measurements performed at least 3 months apart).

### Long-term results

Gelet and associates evaluated long-term outcomes.<sup>12,13</sup> Indeed, this case series includes all the patients treated on his site since the first pilot study for HIFU in prostate cancer.

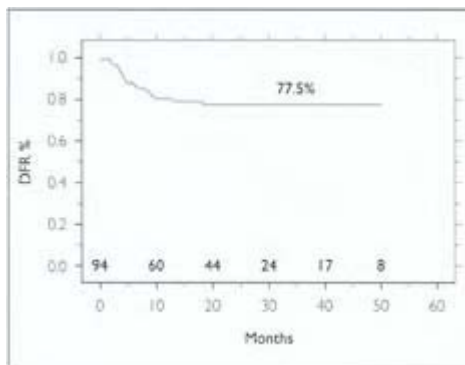
In a recent presentation of his series, results were summarized for a population considered as potentially curable, i.e. presenting with a baseline PSA level  $\leq 10$  ng/ml.<sup>14</sup> These patients ( $n=94$ ) were treated with the successive prototypes of the device, as a primary therapy for localized prostate cancer (T1–2N0–xM0). Patients characteristics before HIFU treatment are presented in Table 45.3. The mean follow-up of the population was 24 months, but included patients with up to 80 months of follow-up.

**Table 45.3** *Patient baseline characteristics for Gelet series with baseline PSA  $\leq 10$  ng/ml and stage T1–T2*

| Characteristic                  | Mean $\pm$ SD   |
|---------------------------------|-----------------|
| Sample size                     | $n=94$          |
| Age (years)                     | $71.8 \pm 5.4$  |
| PSA level (ng/ml)               | $5.84 \pm 2.48$ |
| PSA density (ng/ml)             | $0.20 \pm 0.13$ |
| Prostate volume (ml)            | $34.6 \pm 16.9$ |
| Gleason score                   |                 |
| 2–6                             | $n=58$          |
| 7–10                            | $n=36$          |
| PSA, prostate-specific antigen. |                 |

In this population, an 86% negative biopsy rate was observed, including all the control biopsies performed after HIFU treatment. A PSA nadir  $<0.5$  ng/ml was observed in 70% of the patients. After HIFU treatment, the mean prostate volume was reduced to  $17.6 \pm 9.8$  ml, almost half of the pretreatment volume. In addition, survival curves were calculated with the Kaplan-Meier method, the event being defined as a combination of the biochemical and histologic results: any positive core in control sextant biopsy (whatever the PSA level) or, any biochemical evidence of three consecutive rising PSA levels, or a PSA velocity  $>0.75$  ng/ml/year with or without positive biopsy. According to this definition, the overall disease-free rate was 77.5% at 4 years, the curve evidencing a plateau from 20 months follow-up (Figure 45.7).

When results were stratified according to the Gleason score, an 85% disease-free rate was observed in patients



**Figure 45.7** Kaplan-Meier survival curve for disease-free rate (DFR) for HIFU treatment of low-risk localized prostate cancer. Gelet series with baseline PSA  $\leq 10$  ng/ml, stage T1–T2 with an assessment criteria combining both the histologic and the biochemical patient outcome. (Courtesy of EDAP S.A., Lyon France.)

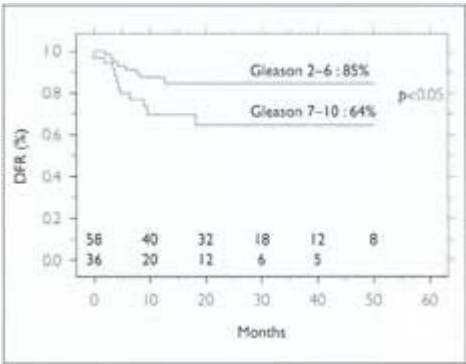
presenting well-differentiated tumors (scores 2–6), whereas the rate dropped to 64% in patients with higher pretreatment Gleason scores (scores 7–10) (Figure 45.8)

Gelet also recently presented the results observed in a larger series ( $n=145$ ),<sup>15</sup> still considering localized prostate cancer patients treated with the Ablatherm as a primary therapy, but with a baseline PSA level up to 30 ng/ml. The patient baseline characteristics are presented in Table 45.4. As previously described, patients were assessed with criteria combining both the histology and PSA stability results. Results were stratified according to the disease-related risk level (definition given in ‘European Multicentric Study’ section), and survival curves were calculated using the Kaplan-Meier method (Figure 45.9). At 4-year follow-up, the observed disease free rates are 84%, 68%, and 47.5% in the low-, intermediate-, and high-risk subgroups, respectively. In all subgroups, the plateau was achieved at 20 months post-treatment.

#### *Standard device performances*

Since 1996, Chaussy and Thüroff have also been involved in the HIFU Ablatherm clinical development. From 1996 to 1999, they treated 184 patients for localized prostate cancer. Follow-up in this population documented an 80% negative biopsy rate and a

normalization of the PSA level in 97% of the patients, including 61% of the patients reaching a PSA nadir of <0.5 ng/ml.<sup>16–18</sup>



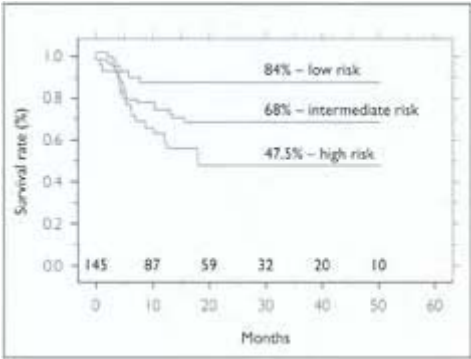
**Figure 45.8** Kaplan-Meier survival curves for disease-free rate (DFR) according to the pretreatment Gleason score for HIFU treatment of low-risk localized prostate cancer. Gelet series with baseline PSA ≤10 ng/ml, stage T1–T2 with an assessment criteria combining both the histologic and the biochemical patient outcome. (Courtesy of EDAP S.A., Lyon, France.)

Since 2000, Chaussy and Thüroff have utilized the standard device: 3 MHz for 5 s for the firing (shots) duration. A total of 144 patients (stage T1–2N0–xM0 without any previous prostate cancer treatment) were treated with the standard device: 65 patients had 12–18 months follow-up, and were assessable for biopsy results and for PSA stability according to the ASTRO definition. Patient baseline characteristics are presented in Table 45.5. During follow-up, control biopsies were systematically performed (mean, 2.25 sextant biopsy set/patient), as well as PSA

**Table 45.4** Patient baseline characteristics (Gelet series with baseline PSA ≤30 ng/ml)

| Characteristic       | Mean±SD   |
|----------------------|-----------|
| Sample size          | n=145     |
| Age (years)          | 71.9±5.4  |
| PSA level (ng/ml)    | 9.2±5.8   |
| Prostate volume (ml) | 34.6±17.0 |
| Risk level:          |           |

Low risk  $n=40$  (27.6%)  
Intermediate risk  $n=64$  (44.1%)  
High risk  $n=41$  (28.3%)  
PSA, prostate-specific antigen.



**Figure 45.9** Disease-free rates stratified according to the risk level. Gelet series with baseline PSA  $\leq 30$  ng/ml: Kaplan-Meier survival curve, with an assessment criteria combining both the histologic and the biochemical patient outcome. (Courtesy of EDAP S.A., Lyon, France.)

**Table 45.5** Patient baseline characteristics (Chaussy and Thüroff series)

| Characteristic            | Mean (range) |
|---------------------------|--------------|
| Sample size               | $n=65$       |
| Age (years)               | 68.5 (51–81) |
| Initial PSA level (ng/ml) | 12.6(1–35)   |
| Prostate volume (ml)      | 22.7 (9–55)  |
| Gleason score             |              |
| 2–6                       | 45.5%        |
| 7                         | 50.0%        |
| 8–10                      | 4.5%         |

PSA, prostate-specific antigen.

measurements every 3 months. Biopsy assessment evidenced an 85.7% negative biopsy rate. Nadir PSA level was generally obtained within 3 months post-HIFU. Median nadir PSA was 0.1 ng/ml, and 92.6% of the patients were still presenting with a stable PSA level at that short-term follow-up. There was a 2% retreatment rate.<sup>19</sup>

*Other prostate cancer indications*

The HIFU treatment is currently under investigation for special subgroups of patients, particularly patients presenting with local recurrence after previous treatment (external radiation therapy, previous radical prostatectomy, and hormonal ablation), and for tumor debulking in locally advanced stages. Results in these subgroups of prostate cancer are too preliminary to draw a conclusion.

In  $n=25$  radiation-failure patients, Gelet et al<sup>20</sup> presented a high post-HIFU negative biopsy rate of 92%, whereas in only 67% of the patients no disease progression was detected at 12 months mean follow-up (range: 3–63 months). While local control of the cancer seems to be easily achieved for these patients, they are often understaged and present with subclinical disease spread, especially in patients with high Gleason grades. It should be mentioned that these patients are at higher risk for HIFU-related adverse effects, such as urinary incontinence or rectal burn.

Similarly, Chaussy and Thüroff presented small series of patients treated with the above indications.<sup>21</sup> In patients with recurrence after external radiation, after surgery, or after hormonal ablation, they also observed promising local control of the disease, with 78%, 72%, and 79% negative biopsy rates, respectively. They also noted an increased treatment-related morbidity in patients who had undergone a previous local treatment, i.e. in patients treated with HIFU after surgery or external radiation, but not in patients who had been first treated with hormones.

For patients with locally advanced prostate cancer, Chaussy and Thüroff also presented the local HIFU results observed in 24 patients.<sup>22</sup> After a single HIFU session, 50% of the patients presented with negative biopsies, while the tumor mass was reduced by 80% in patients with residual local cancer post-HIFU. The use of HIFU as a palliative local treatment of the primary cancer site to delay disease progression and defer hormone treatment (potentially delay hormone resistance) is nevertheless open to debate.

**Safety results**

HIFU-related morbidity has also evolved through successive device prototypes, while we have simultaneously optimized the treatment procedure.

During the Pilot Study II, urethrectal fistulas due to direct rectal burn occurred, and this adverse effect was considered not acceptable for a minimally invasive treatment. As a consequence, additional safety features were progressively implemented, as previously described.

In parallel with the device evolution, the operators also optimized the treatment procedure, in order to minimize the second most severe risk: the occurrence of stress incontinence due to injury of the external sphincter. For this purpose, a safety margin was defined for the apical treatment, leading to a decrease in the occurrence of stress incontinence without an increase in (apical) residual cancer in this region.<sup>16–18</sup>

In 2000, Chaussy and Thüroff described the impact of this device evolution.<sup>23</sup> All patients were systematically assessed post-HIFU with a 50-item questionnaire, which included all the theoretically possible treatment-related complaints or adverse effects. The results described for the ‘last 100 patients’ are summarized in Table 45.6. The most frequently observed side-effects are the absence of ejaculation, which is generally not a

concern in an elderly population, and the immediate post-treatment urinary retention. This post-treatment retention is first due to the edema of the gland, then may be prolonged in the case of prostate tissue sloughing.

To reduce the catheter time after HIFU, and to improve the patient comfort in the immediate follow-up, Vallancien performed a transurethral resection of the prostate (TURP) immediately prior to the HIFU treatment, under the same anesthesia. He demonstrated that TURP does not affect the treatment performance. According to this strategy, Vallancien observed that the mean catheter time went from 9.1 days to 3.3 days.<sup>13,24</sup> The impact of a combined TURP+ HIFU treatment was also studied by Thüroff and Chaussy,<sup>25</sup> who observed a reduction of the suprapubic catheter time from 37 days in mean after HIFU to 7 days

**Table 45.6** *Treatment related adverse effects*

| Type of side-effect                            | Occurrence in the last 100 patients |
|--|-------------------------------------|
| Death (intra- and post-operative)              | 0                                   |
| Fistula  | 0                                   |
| Rectal wall burn                               | 0                                   |
| Hemorrhoidal pain                              | 1                                   |
| Stress incontinence:                           |                                     |
| Grade I (average 27 days)                      | 9                                   |
| Grade II (average 32 days)                     | 2                                   |
| Grade III (after TURP)                         | 1                                   |
| Urge incontinence                              | 0                                   |
| Urgency  | 7                                   |
| Urinary tract infections                       | 13                                  |
| Significant hematuria                          | 0                                   |
| Immediate post-treatment retention             | 100                                 |
| Total erectile dysfunction                     | 22                                  |
| Absence of ejaculation                         | 100                                 |
| TURP, transurethral resection of the prostate. |                                     |

after TURP+HIFU. The pre- and post-treatment IPSS scores remained unchanged after HIFU (before 5, after 5, in mean), but were improved after TURP+HIFU (before 5, after 2). It should be noted that the patient morbidity after the combined TURP+HIFU treatment was similar to that after a standard (classical) TURP.

Chaussy and Thüroff<sup>16-18</sup> recorded that, after a complete treatment of the gland, two-thirds of the previously potent patients will develop erectile dysfunction. When the prostate cancer seems to involve only one lobe, they proposed a nerve-sparing treatment, excluding 5 mm rim of tissue on the contralateral side near the neurovascular bundle. Utilizing this technique the incidence of erectile dysfunction dropped to one-third of the cases. However, a 15% higher cancer recurrence rate developed in these patients. In these cases, an HIFU retreatment may be performed. It should be noted that these potency results were observed in a population with a mean age of 72 years old.

In conclusion, it can be stated that due to the improvements in the device and in the clinical procedure, severe side-effects such as fistula and grade III stress incontinence did not occur when treating a patient with HIFU as a primary therapy for prostate cancer.

## Discussion and Conclusion

Overall, these HIFU Ablatherm results are often considered difficult to interpret because different device prototypes, different technical parameters, and different clinical procedures were used during the treatment's development period. On the other hand, all these changes were progressive optimization, without sharp modifications, and should be considered as fine tuning. This has led to a standardized device as well as a standardized treatment procedure.

The main advantages of the HIFU treatment may be summarized as follows:

- The learning curve is short for a urologist experienced in transrectal ultrasound (approximately 10 patients according to the experience of the new user sites).
- As a minimally invasive treatment, HIFU may be performed under spinal anesthesia. The HIFU-related morbidity is low, and the post-treatment management is easy. The evening after the HIFU session, the patient returns to normal food, does not need any analgesic medication, and may be discharged the day after with a catheter in place, or a few days later without catheter.
- The nadir PSA is generally obtained within 3 months after HIFU treatment.
- The HIFU treatment may be performed in patients with previous TURP.
- The HIFU treatment may be repeated during patient follow-up. For safety aspects, at least a 6-month interval is recommended between the two HIFU sessions.
- The HIFU treatment may be performed for local recurrence after previous prostate cancer therapy.
- In the case of local recurrence after HIFU, the patient may still receive a potentially curative treatment (second HIFU session or external beam radiotherapy).

The CE mark, the Ablatherm device, is indicated for the treatment of localized prostate cancer, as a primary therapy in T1–T2 patients, or for the treatment of local recurrence after external beam radiation or after prostatectomy.

In our practice, patients selected for the HIFU Ablatherm treatment are:

- patients who are not candidates for surgery due to their age or comorbidities
- patients who are poor candidates for surgery due to the local conditions (history of prostate surgery or radiation) or with a risk for positive margins
- patients refusing invasive surgery.

As of June 2002, more than 2000 patients have been treated with HIFU for prostate cancer in Europe.

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## Cryotherapy of localized prostate carcinomas

Moritz Braun, Stefan Wolter and Udo H Engelmann

### Introduction

Therapy for localized adenocarcinoma of the prostate is currently undergoing a marked transformation. In addition to retropubic prostate vesiculectomy, the standard operation for many years, perineal and laparoscopic prostatectomy have established themselves recently as alternative treatments. Unfortunately, preoperative diagnostics, especially with regard to imaging, have not kept pace with the development of these new surgical techniques. This means that a complete removal of the entire tumor is possible from a curative point of view, even if this entails serious side-effects (e.g. incontinence). Moreover, in the face of demographic changes in the population of the Western industrialized nations, the quality of life of older people is increasingly becoming a focus of attention. One aspect of quality of life is the maintenance of sexual function. But current therapeutic surgical procedures are often accompanied by the loss of erectile capability, especially since it is impossible to foresee the exact anatomic situation prior to an operation and thus to guarantee maintenance of postoperative sexual function.

For these reasons, other forms of therapy have been sought that entail a lesser degree of side-effects. Technical improvements in radiation therapy, enabling the establishment of external and/or internal radiation—brachytherapy and high dose rate (HDR) afterloading—have made these viable curative therapeutic procedures options to surgery. However, these are subject to strict limitations with regard to the spread and histologic differentiation of the prostate carcinoma. Furthermore, due to the high amount of radiation energy applied, the procedures cannot be repeated. Failure rates ranging from 10 to 30% have been variously cited in the literature.<sup>1–3</sup> Especially for these ‘radiation therapy failures’, cryotherapy constitutes a valid therapy alternative.

### Mechanism of action

In cryotherapy an interstitial application of cold leads to the necrosis of prostate cells. The extracellular water crystallizes, followed by a hyperosmolar cellular dehydration. As a result, the cells shrink as the membranes and other cell compartments are destroyed. Within a few minutes the increased intracellular electrolyte concentration is high enough to induce cell decline. This procedure is known as ‘solution effect injury’ and usually leads to the death of the affected cells. A further functional mechanism that always leads to cell necrosis is intracellular crystal formation. Both processes are brought about in the

course of cryoablation, depending on the speed with which freezing takes place. Whereas intracellular crystallization appears with a sudden and extreme drop in temperature ( $-40^{\circ}\text{C}$ ), the 'solution effect injury' is induced by higher temperatures (from  $0^{\circ}\text{C}$ ) and a slower freezing speed.<sup>4-8</sup>

## History

In principle, cryoablation is a relatively old therapeutic procedure. James Arnott in England had already reported on its use as early as 1865. Around 1960 the first generation of cryoablation devices were introduced for treatment of the prostate; they were used to treat benign prostatic hyperplasia (BPH). They used liquid nitrogen for freezing the tissue. Due to the serious side-effects, however, cryotherapy eventually fell into disuse. Then, in the early 1990s, the second generation of devices came onto the market. These work according to the 'Joule-Thomson principle' (gas expansion) and enable significantly better control of the freezing process. In the earlier devices the relatively large needle diameter had made an exact control of the freezing process and the generation of a uniform temperature field virtually impossible.<sup>9</sup>

Today the third generation of devices is being introduced onto the market. With this new technique, similar to that used in interstitial radiation, many fine needles (about 20) are placed perineally, with the exact placement monitored via ultrasound. Temperature probes are used to ensure that neighboring organs (urethra, rectum) are protected from injury, while a consistent low-temperature field can be created to freeze the prostate carcinoma effectively<sup>10,11</sup> (Figure 46.1).

## Indications and contraindications

### *Indications*

Generally, cryotherapy is indicated in cases of localized adenocarcinoma of the prostate (pT1/2, Gleason score  $\leq 6$ ). The prostate volume should be under 40 ml. Metastatic spread should be excluded.

A distinction is made between primary and secondary indications.

A primary indication exists for those patients who, due to severe comorbidities or a previous treatment (e.g. radiation of a rectal carcinoma), cannot undergo surgery. An indication is also given for patients who refuse surgical intervention and express explicit preference for this kind of curative therapy, always on the condition that the abovementioned criteria are fulfilled.

Now that various curative radiation options have been introduced (brachytherapy, high dose of radiation (HDR) afterloading, etc.) the possibility of a secondary indication for cryotherapy has taken on a new importance. Depending on which literature is consulted, local failure rates following radiation therapy range between 10 and 30%.<sup>1-3</sup> Because of the HDR employed, repeated treatment is usually out of the question, making cryotherapy a valid treatment option in such cases. Patients are classified as radiation therapy failures

who show on three consecutive PSA (prostate-specific antigen) measurements a rise and histopathologic evidence of vital tumor cells by means of a prostate biopsy.

### *Contraindications*

In addition to evidence of metastasis or an unfavorable histopathologic classification (e.g. Gleason score > 6), a previous prostate operation, such as transurethral resection of the prostate (TURP) or suprapubic adenectomy of the prostate (SPE), should also be viewed as a



**Figure 46.1**

## The development of cryoprobe.

contraindication for cryotherapy treatment, since the resulting small prostate volume to be expected in such cases (<20 ml) and postoperative adhesions do not allow for reliable protection of the rectum.

Furthermore, patients with a urothelial carcinoma should not undergo cryotherapy, since this could cause unnecessary complications if a cystectomy should be required at a later date. In such cases it should be determined whether, in light of a histologically unfavourable urothelial carcinoma in combination with a localized prostate carcinoma, primary cystoprostatectomy might be the method of choice.

Since cryotherapy cannot be expected to yield any improvement in micturition, we also exclude patients with marked obstructive micturition difficulties (including patients on catheter drainage). In these cases we introduce primarily an antiandrogen therapy and monitor voiding patterns after at least 3 months of treatment. If at this time, post-void residual volume is low, cryotherapy can be carried out.

In our own clinic we have defined a few additional relative contraindications: here we were guided by safety considerations, so as not to bring discredit to a new, not yet fully established therapeutic procedure. Hence they are relative not absolute contraindications, and must be assessed on an intra- and inter-individual basis:

- inflammatory intestinal diseases
- prior operations in the small pelvis
- bladder diverticula
- coagulopathies (including iatrogen-based).

## Preoperative diagnostics

Preoperative diagnostics must first document adenocarcinoma of the prostate by means of a prostate fineneedle biopsy. Histopathologic differentiation (Gleason score) should not be higher than 6. Transrectal ultrasonography is used to determine prostatic volume, usually during the prostate biopsy. A volume of 40 ml should not be exceeded. Further general diagnostic tests follow, including computer tomography (CT) of the abdomen and small pelvis, as well as a bone scan. We also carry out pelvic lymphadenectomy (laparoscopic or minilap) on men with PSA  $\geq 15$  ng/ml, Gleason score  $\geq 8$  disease, or TNM (tumor-node-metastasis) stage T2b or greater. If any metastasis is observed, cryotherapy is not carried out.

## Preoperative preparation and execution

Preoperative preparations are not any different from those conducted for brachytherapy or HDR afterloading patients.

Cryoablation of the prostate is undertaken as a one-time or, rarely, two-time operation under general or regional anesthesia, based on the technique described by Onik in 1989 and 1993.<sup>12,13</sup> During the operation the patient is in the dorsal lithotomy position. To

prevent infection, ciprofloxacin 2×200 mg daily is applied both during and after the procedure. The operation begins with a cystoscopy for orientation. The bladder is then filled with at least 250 ml NaCl 0.9% and a suprapubic catheter is inserted. In our experience any pre-existing obstructive problem is likely to increase in the first postoperative weeks due to reactive swelling, making the suprapubic catheter a necessity during this phase to ensure that the bladder remains free of any residual urine.

After the cystoscope is removed, a transurethral heat catheter is placed in order to protect the prostatic urethra from any cold-induced damage. This allows for a significant reduction in the rate of complications with regard to excretion of necrotic urethral particles or subvesical obstructions. A pump system constantly circulates body temperature fluid through the transurethral heat catheter, serving to ward off coldness in areas that should be protected. Methylene blue solution may be added to this irrigation fluid. A blue coloration of the urine leaving the suprapubic catheter would then show the surgeon that the heat catheter had been damaged in the course of the prostate biopsy. In order to reduce the risk of a catheter defect, it is recommended that the heat catheter first be blocked when the prostate puncture is complete.

A transrectal ultrasound (TRUS) probe is fixed in place. Precise measurements of the prostate are taken and the correct insertion of the puncture needles planned. Monitoring the procedure continually via ultrasound, a puncture aid (template) is used to help place up to 20 echogenous puncture needles perineally in the prostate tissue. The hyperechogenous needles are then brought into the desired position and their placement checked via ultrasound in the sagittal and transversal planes. The probes should be placed from anterior to posterior, in order to enable an optimal sonographic visualization (Figures 46.2–46.4). Several separate thermoprobes can be placed inside or outside the gland in order to facilitate more precise control of the freezing process (Figure 46.5). In addition to allowing the surgeon to make sure the required temperature is maintained for a complete cold-induced necrosis (monitoring of effectiveness), this also helps to prevent rectal fistulae and protects the vasomotor nerve bundle responsible for maintaining erectile ability.



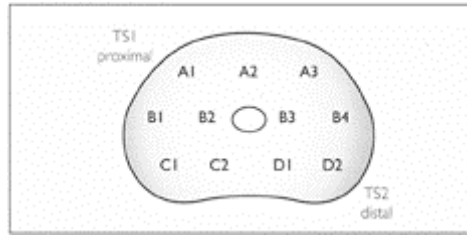
**Figure 46.2**

Placement of the upper cryoprobe row.



**Figure 46.3**

All cryoprobes placed.



**Figure 46.4**

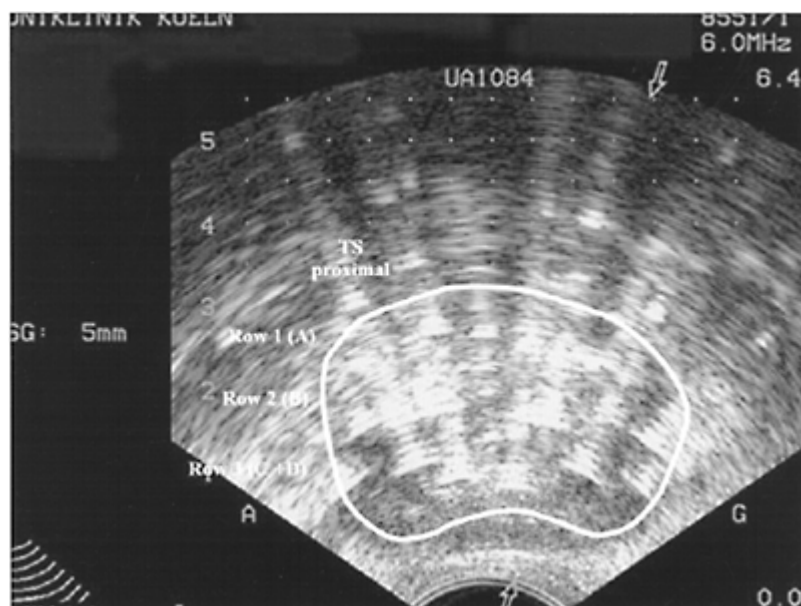
Schematic placement of the cryoprobes (A–D), and possible position of the thermosensors (TS).

Technical advances in cryotherapy techniques have made it possible to freeze or thaw individual or grouped cryoprobes independently of one another, allowing for a high degree of localized temperature control.

Once all cryoprobes have been placed, they are activated sequentially from anterior to posterior, so that the resulting ice balls melt together. As the therapeutic tissue temperature zone of  $-40^{\circ}\text{C}$  is reached, it is possible to monitor the growing ice ball exactly by means of the high-resolution TRUS and based on the temperature readings from the thermoprobes. The freezing phase is maintained for about 10–15 min.

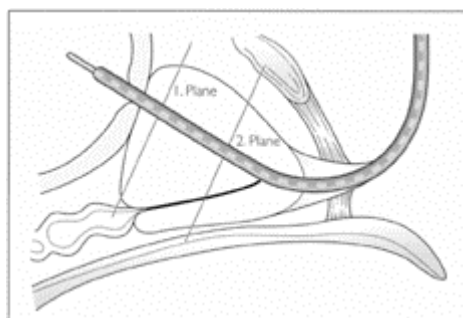
The hyperechogenous boundary of the ice ball can be followed on the ultrasound image, while the thermoprobes register temperatures in the area of the prostate capsule. The rectal wall can usually be monitored quite well sonographically. Upon completion of the 15 min freezing cycle, the cryoprobes are switched off for about 10 min—initiating the thawing process. The cryoprobes are not warmed actively for the thawing phase, in order to achieve slower, more natural thawing. A second freezing cycle is carried out in the same way to complete the ‘double freeze’ procedure. Depending on the length of the prostate, the cryoprobes are then pulled out somewhat and the ‘double freeze’ process is repeated apically. Experience shows that time can be saved by first carrying out the freezing process basally and then apically, and then repeating the process. Thus, the time required for natural basal thawing is used for apical freezing, and vice versa (Figure 46.6).





**Figure 46.5**

Ultrasound after placement of all cryoprobes.



**Figure 46.6**

distal (2. Plane) treatment. Placement of the cryoprobe tips for proximal (1. Plane) and

After cryoablation is completed, the probes are removed. The transurethral heat catheter should remain in situ for an additional 15 min. Manual compression of the perineum and

subsequent application of a compression bandage helps to prevent the development of hematomas.

### **Technical equipment**

Currently, three different companies manufacture cryoablation devices. All instruments are equipped with a thawing device so that the ablation can be executed in multiple cycles, enhancing its effectiveness. At present we are using the SeedNet system produced by the Galil Medical, together with multifrequent, biplanar TRUS for three-dimensional visualization of the prostate. This system contains needles with a smaller diameter (17-gauge), so that more needles can be used to effect a more even distribution of temperature. In addition, it is possible, for protecting sensitive structures (e.g. the rectum), to place thawing needle(s). The ultrasound probe is fixed onto a stepper unit with a 17-gauge template. Ultrasound technology is the area that currently offers most room for progress in the treatment technique. Now that three-dimensional ultrasound is possible, anatomic idiosyncrasies of the prostate can be seen more easily, leading to more individualized planning of the cryotherapy procedure.<sup>14</sup> Combining ultrasound with a Doppler signal would be even more helpful in identifying possible carcinoma growth beyond the confines of the prostate itself, as well as in localizing the periprostatic neurovascular bundle.<sup>15</sup>

### **Operative access and helpful tips**

#### *Operative access*

As already described above, now that TRUS is available, perineal access makes the most sense. In some exceptional cases, when for primary treatment a radical perineal prostatectomy is attempted, but during the operation a locally too advanced tumor stage is found (apex or neurovascular bundle infiltration, etc.), an 'open' cryoablation may be performed.

#### *Neoadjuvant antiandrogen treatment*

The size of the prostate is an important criterion in determining whether cryotherapy is indicated. In one study, 26 of 43 patients who underwent cryotherapy were treated preoperatively with a complete androgen blockade. The indication for this treatment was a prostate volume of >40 ml. The androgen blockade was carried out for 3 months prior to the operation and the volume changes monitored by means of regular ultrasound checks. Postoperatively, these patients demonstrated comparable oncologic results to those who did not undergo androgen therapy.<sup>16</sup> Our results were similar to those achieved by Bahn et al. They also observed a significant reduction in volume (33.3 to 21.3 ml), with a progression rate of 13.3%.<sup>17</sup> In their group of 119 patients, Cohen and coworkers were able to demonstrate an advantage for those receiving preoperative therapy.<sup>18,19</sup> In summary, it can be stated that preoperative antiandrogen treatment expands the

possibilities of cryotherapy. Whether or not this creates a survival advantage for these patients needs to be evaluated in the course of further studies.

### *Enhancing effectiveness*

The reduction in size of the cryoneedles used not only offers the advantage that with a larger number of needles a more even temperature field can be generated but it also harbors the danger of an incomplete ablation.<sup>20</sup> The injection of antifreezing proteins (AFP) might prove helpful here. In an experiment using animals, Muldrew and coworkers were able to demonstrate that subcutaneous injection of AFP prior to cryoablation led to a significant improvement in ablation results.<sup>21</sup>

## **Intra- and postoperative complications**

### *Incontinence*

Postoperative incontinence is certainly a parameter for the patient's continued quality of life. There are diverse claims with regard to this factor in the literature. While in our study group 69% of previously radiated patients were incontinent, we found that only 1% of the patients receiving cryotherapy as primary treatment suffered from this complaint.<sup>22</sup> Long and coworkers had similar results.<sup>23</sup> The explanation probably lies in the cumulative injury to the sphincter externus. For such patients the preoperative performance of a sextant biopsy (if this has not already been done) is to be recommended. Histopathologic examination of the biopsy specimen close to the apex should preferably show no infiltration of the known prostate adenocarcinoma. This would allow for a larger safety margin protecting the sphincter region during cryoablation.

Patients who manifest marked obstructive voiding symptomatic preoperatively will under some circumstances experience an aggravation of these symptoms postoperatively, even to the point of dysuria. This represents a dilemma for the physician: on the one hand, an indication for the performance of cryotherapy exists; on the other hand, one will probably need to perform a TURP postoperatively, involving a high risk for incontinence. The physician has no choice here but to perform this subsequent surgery after an interval of 3 months, and to carry out the operation sparingly. In the interim, the patient needs a suprapubic catheter, maintaining a micturition log and documenting amounts of residual urine.

### *Injury to the rectum*

One problem feared in association with cryotherapy is the possibility of injury to the rectum, accompanied by the development of a rectourethral fistula. The probability of this occurring is relatively high in those patients with locally advanced tumor growth or those who have undergone radiation. As a preventive measure, the injection of saline solution into Denonvilliers' fascia is recommended. This increases the distance between rectum and prostate, thus minimizing the risk of rectal injury. Onik was able to demonstrate on more than 200 patients that this commonly dreaded complication could

thus be avoided.<sup>24</sup> In 25 other patients who experienced a relapse following radiation, this technique also served to preclude any rectal injuries.<sup>25</sup>

Using needles with small diameter, it is possible to place two of them in (or beside) the rectum wall. We are also able to avoid rectal fistulas with active thawing, during the freezing circle. This also works in already-radiated men.

### *Impotence*

The loss of potency following cryotherapy is relatively frequent. Various authors have reported impotence rates of around 80–90%.<sup>26–28</sup> This is one of the major disadvantages of cryotherapy, compared to radical nerve-sparing prostatectomy. When cryotherapy is carried out thoroughly and completely with regard to tumor control, the paraprostatic tissues are inevitably affected, and with them the corresponding vasomotor nerve bundles. Hence, some authors define a postoperative loss of potency as an expression of a successful ablation, especially in cases of large tumor volume with possible paraprostatic extension. Even if nerve regeneration appears to be a possibility in some cases, physicians have recently begun to search for ways of performing a more ‘nerve-sparing cryotherapy’. An important role will probably be played here, as mentioned above, by the improvement of sonographic representation. The introduction of three-dimensional sonography enables a better visualization of the prostate and therefore a more precise placement of the cryoprobes.<sup>29</sup> It would thus seem to be possible to identify the vasomotor nerve bundles and safeguard them as required.

In a small group of 9 patients, Onik and co-workers were able to maintain erectile ability in 7 patients solely by protecting the vasomotor nerve bundle on the side opposite the tumor. Their selection criteria for a ‘nerve-sparing cryotherapy’ are:

- unilateral tumour invasion
- small tumour volume.

They were thus able to avoid compromising their oncologic results.<sup>30</sup>

### *Injury to the urethra*

Prior to the introduction of the urethral heat catheter, problems with postoperative changes in the urethra, in combination with marked dysuria and urethral excretion of tissue fragments were frequent concerns. The heat system has been in use since 1996, serving to protect the urethral mucosa and prevent necroses from forming there. This has rapidly reduced urethral complications, without however precluding them altogether (33% in our patients). De la Taille and Katz left the heat catheter in situ for a further 2 hours and were thus able to completely eliminate urethral complications.<sup>31</sup>

## **Results**

In our own study we were able to demonstrate that the postoperative PSA value for 58% (28/48) of patients was under 0.5 ng/ml 6 months after the cryoablation, and 79% (38/48) of the patients had a negative follow-up biopsy. In this same patient group, treatment

success could also be shown to be dependent on tumor stage as well as on tumor differentiation.<sup>32</sup>

Our results are essentially in keeping with those of others who have investigated this therapy, even at a time when we were still using a second-generation cryoablation device<sup>8,28,33,34</sup> (Table 46.1). Overall, one can state that our initially good results have been confirmed, even after longterm observation (up to 5 years). It can thus be established that, from the standpoint of oncology, cryotherapy in patients with primary indications yields results comparable to those achieved through surgical procedures or brachytherapy. As to postoperative morbidities, our patient group showed the following results: impotence could be observed after 6 months in 77% (27/35 preoperatively potent men) of patients. Interestingly enough, during further follow-up, 3 of these men regained erectile potency adequate for normal sexual intercourse, without receiving any sort of erection-promoting therapy. Thirtythree percent (19/57) of the men suffered from postoperative dysuria in combination with ‘sloughing’. A further 13 of the 57 patients (22%) experienced prolonged urine retention, which had to be treated in 6 patients (10%) using TURP. Incontinence developed in 9% (5/57) of the patients, traceable in 2 of the patients to a sphincter injury; the other patients were treated satisfactorily by conservative management. Fortunately, we observed no rectourethral fistulae. This spectrum of postoperative complications is comparable with that evaluated by Long and co-workers in their large-scale multicenter study. They compared the frequency of complications with those following radiation therapy and found a similar distribution<sup>28</sup> (Table 46.2).

A special importance can be attributed to studies of ‘salvage cryotherapy’, i.e. as therapy for secondary indica-

**Table 46.1** *Cryosurgical ablation series of prostate cancer of primary indications*

| Main author             | Number of patients | PSA <0.5 ng/ml      | Negative postoperative biopsy |
|-------------------------|--------------------|---------------------|-------------------------------|
| Bahn <sup>33</sup>      | 590                | 63.3%               | 87%                           |
| Leibovici <sup>11</sup> | 12                 | 66.6%               | n.i.                          |
| Long <sup>28</sup>      | 975                | 36–60% <sup>a</sup> | 82%                           |
| Ellis <sup>34</sup>     | 75                 | n.i.                | 84%                           |

<sup>a</sup>According to risk group (low, medium, high), n.i.=not investigated.

tions. Two decisive aspects come into play here. For one thing, after radiation therapy has failed, the patient finds himself in a difficult predicament. An operation is often not an option, either because the patient himself has refused surgical intervention as primary therapy or because accompanying illnesses originally precluded more extensive surgery. Now, either a much more difficult operation ensues, or, as an alternative, a long course of palliative androgen-blocking medication. This often does not correspond with the patient’s own wishes, however, and is also a poor solution economically; compared with the high costs of long-term medication, the expense of performing cryotherapy will be amortized within 2 years. Studies of patients who received prior treatment show that in these cases results can be achieved that are just as good as those in patients for whom cryotherapy represents the primary intervention<sup>35–38</sup> (Table 46.3). Therefore, for our clinic, where cryotherapy is not used as often as radiation (external or interstitial), the secondary indication is actually the main indication. Even if the rate of postoperative

morbidity seems to be somewhat higher, this should surely be regarded as acceptable in view of the excellent oncologic outcomes.

**Table 46.2** *Postoperative morbidity: multicenter study (cryotherapy) vs literature overview (radiation)*

| Symptom               | External radiation | Brachytherapy | Cryotherapy |
|-----------------------|--------------------|---------------|-------------|
| Incontinence          | 0–13%              | 0–5%          | 7.5%        |
| Impotence             | 37–70%             | 10–40%        | 93%         |
| TURP                  | 0–3%               | 0–4%          | 13%         |
| Rectourethral fistula | 1–9%               | 0–7%          | 0.5%        |

Source: reproduced with permission from Long et al.<sup>28</sup>

**Table 46.3** *Cryosurgical ablation series of prostate cancer for secondary (salvage) indications*

| Main Author                | Number of patients | PSA <0.5 ng/ml | Negative postoperative biopsy |
|----------------------------|--------------------|----------------|-------------------------------|
| Ghafar <sup>35</sup>       | 38                 | 74%            | n.i.                          |
| Chin <sup>36</sup>         | 118                | 96%            | 94.1%                         |
| Izawa <sup>37</sup>        | 145                |                | 79%                           |
| de la Taille <sup>38</sup> | 43                 | n.i.           | 66%                           |

Source: reproduced with permission from Long et al.<sup>28</sup> n.i.=not investigated.

## Conclusion

Based on the results of clinical studies carried out by the US Health Care Financing Administration (HCFA), cryotherapy has been approved for primary and secondary (radiation failure) therapy of adenocarcinoma of the prostate in the United States. For the same indications cryotherapy got the FDA (Food and Drug Administration) Approval. Hence, it can no longer be regarded as an experimental therapeutic procedure.

Apart from the fact that cryotherapy represents a valid curative therapy option for localized tumors, answering the justifiable desire of many patients for a minimally invasive form of treatment, cryotherapy also makes sense from an economic standpoint. When radiation therapy fails, often the only solution that has to be discussed is antiandrogen treatment with, at best, a palliative expectation.

In our view cryotherapy of the localized prostate carcinoma is still no substitute for radical prostatectomy, which remains the standard therapy for this condition. Because of the long progression time for prostate cancer (up to 15 years), a balanced assessment can only be made following further studies. An important adjunct requirement for this therapy is that all cryotherapy patients be monitored in accordance with standardized parameters over long periods of time following treatment.

With regard to radiation, cryoablation can already today be considered a genuine alternative. This procedure is particularly interesting for clinics and medical centers that do not offer radiation therapy and have no license to handle radioactive substances, but still wish to offer their patients a promising semi-invasive therapeutic procedure.

In the form of salvage therapy (for secondary indications), cryotherapy represents a treatment alternative that is of great value to patients; also, from an economic point of view, it should be actively endorsed.

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## Hyperthermia in the treatment of localized prostate cancer

Serdar Deger

Prostate cancer is the fourth most common cancer in men worldwide. In the United States it is the most common cancer diagnosis and the second most common cause of cancer-related mortality.<sup>1</sup> The treatment of prostate cancer creates considerable controversy due to the vast array of different options currently available. Radical prostatectomy effectively eliminates cancer in a large number of patients. However, experience in the last decade has shown that the radical surgery does not always result in local tumor control in patients with capsule invasive prostate cancer.<sup>2</sup> Major advances in the radiotherapeutic treatment of prostate cancer have been realized with the development of linear accelerators, conformational techniques, transrectal ultrasound imaging, and insertion of radioactive materials directly into the prostate.<sup>3-5</sup> In spite of the improved radiation therapy tumor control of locally advanced disease, under 70% of T2c-T3 tumors with Gleason score less than 6 are not adequately treated.<sup>6</sup>

The uncertain results and possible side-effects of current treatment options have created fertile ground for innovative strategies in the treatment of prostate cancer.

Normal tissue tolerates temperatures of 41–44°C. The absence of regulatory mechanisms in malignant tissue can result in tissue damage from necrosis if the same temperature range is used. The exact cause of cell death from hyperthermia is not yet completely understood. Changes in cell metabolism that relate directly to the Krebs cycle, lipid metabolism, oxidative phosphorylation, and glycolysis may be involved. In addition, an inhibition of cellular repair mechanisms, an enhanced direct cytotoxicity in radiation-resistant phases of the cell cycle (G2 and S phases), and damage to the cell membrane and the cytoskeleton have been postulated as possible mechanisms of action.<sup>7</sup> Raaphorst et al first reported cytotoxic effects of hyperthermia in mammalian cell lines in 1979. The extent of the hyperthermic cytotoxicity depends on the thermal dose, which is a function of the amount of heat administered and the duration of exposure to heat.<sup>8,9</sup>

Hyperthermia has been demonstrated to improve clinical outcomes, including survival, in several phase III trials for different types of malignancies.<sup>10-14</sup> The effects of irradiation can be enhanced by hyperthermia of tissues due to its additional cytotoxicity (from 42.5 to 43°C) and sensitization (from 40.5 to 41°C). Cytotoxicity induced by hyperthermia appears to be enhanced under microenvironmental conditions such as reduced perfusion, acidosis, and reduced cell metabolism.<sup>15,16</sup>

Mittelberg et al reported synergy between hyperthermia and radiation. They did not observe radiation resistance due to thermotolerance in a prostate cancer cell model. They suggested that injury to heated and irradiated prostate cancer cells was possibly due to separate mechanisms working simultaneously.<sup>17</sup>

Peschke et al used three different sublines of a Dunning rat prostate carcinoma R3327 model (anaplastic, moderately differentiated, and well differentiated) to show that local tumor hyperthermia alone induced growth delay in both differentiated tumors, while the anaplastic tumor subline did not respond. Combining hyperthermia with radiation, cell damage in anaplastic tumors improved.<sup>18,19</sup> This study group also worked on radiation dose rate, sequence, and frequency of heating, and found a clear thermal enhancement of low dose rate irradiation, with maximal sensitization when hyperthermia was given just before irradiation.<sup>20</sup>

Li and Franklin studied apoptosis in irradiated and heated PC-3 prostate cancer cells. They found that apoptosis was an important mode of death in heated cells, but not in irradiated cells. No significant apoptosis was observed when cells were heated at 42°C for 240 min. Thus, a heating temperature of 43°C and above may be required to induce significant apoptosis in a clinically feasible duration of time. They concluded that apoptosis-inducing modalities such as hyperthermia may supplement radiation therapy in the future management of prostate cancer.<sup>21</sup>

Different heat delivery systems for the prostate have been described. Achieving therapeutic temperatures in the prostate is difficult. Because of their acute toxicity noninvasive techniques such as radiofrequency phased arrays limit the amount of heat that can be applied.<sup>22</sup>

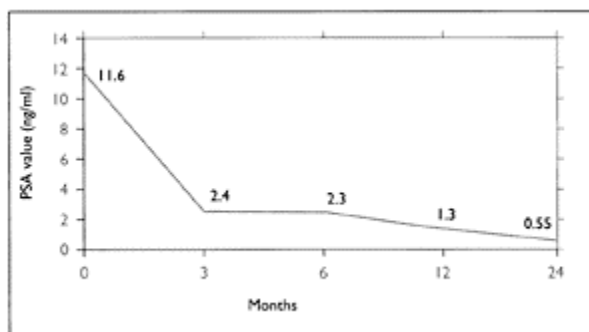
The combination of hyperthermia with radiation therapy to treat prostate cancer has been investigated since the 1970s, but several study results have been disappointing.<sup>23–25</sup> Anscher et al<sup>23</sup> combined 44–46 Gy EBRT (external beam radiation therapy) with regional hyperthermia of  $\geq 42^\circ\text{C}$  and reported 3-year disease-free survival rates of only 25% in patients with stage T3–T4, mean PSA value of 69 ng/ml, and mean Gleason scores ranging from 7 to 9.

One way to overcome some of the limitations of external heating systems for the prostate is by direct heating of the prostate through interstitial hyperthermia. Advantages of the interstitial invasive techniques of hyperthermia application compared with noninvasive approaches include:

1. defined energy application in the tumor with protection of rectum and bladder
2. more effective local therapy
3. homogeneous energy distribution and better temperature distribution.

One strategy of interstitial heating systems is transrectal hyperthermia. In the early 1990s, a transrectal ultrasound device was developed, especially for prostate hyperthermia.<sup>26,27</sup> A phase I trial combining transrectal hyperthermia with EBRT (standard radiotherapy to the prostate and periprostatic tissues, using a four-field approach with 1.8–2 Gy daily fractions applied 5 times/week to a total dose of 67–70 Gy) was performed at the University of Arizona by Fosmire et al.<sup>28</sup> The ultrasound power was delivered from a water-cooled 16-element partial cylindrical intracavitary array. Fosmire et al reported that transrectal ultrasound hyperthermia was well tolerated by the patients. However, the average temperature (measured using thermocouples inserted into the prostate) was only  $41.9 \pm 0.9^\circ\text{C}$  over 30 min. Using this device, a phase II trial of hyperthermia and EBRT with or without hormonal therapy for locally advanced prostate cancer was performed by Hurwitz et al on 9 patients with clinical T2b–T3b prostate cancer.<sup>29</sup> The total radiation dose delivered was 6660 cGy  $\pm 5\%$  of the prescribed target volume using a three-

dimensional conformal technique. A four-field technique was used for all patients. Two hyperthermia treatments are administered at least 1 week apart during the first 4 weeks of radiation. Five patients also received hormonal therapy. Median temperature for each treatment was 40.8°C. Mean cumulative equivalent minutes, for which 43°C temperatures were measured, was 3.4 min ( $0.5 \pm 13.1$  min). Rectal wall temperature was maintained at  $\leq 40^\circ\text{C}$ . Treatment duration was limited in three of 17 sessions due to positional discomfort. Using the National Cancer Institute Common Toxicity Criteria, acute toxicity was limited to grade 1. No excess toxicity was noted with a full course of radiation therapy  $\pm$  hormonal therapy. Using this described method in 2002,<sup>30</sup> this study group reported about 30 patients having rectal toxicity. A cooling water bolus was maintained between 33°C and 37°C to keep the maximum rectal wall temperature within treatment guidelines. Rectal toxicity was correlated with maximum allowable rectal wall temperature of  $>40^\circ\text{C}$  (7 of 11 patients had an acute grade 2 proctitis).



**Figure 47.1**

PSA (prostate-specific antigen) value follow-up of the Charité Group.

Using the same ultrasound device, Raaymakers et al<sup>31</sup> reported no additional long-term toxicities with the combination of hyperthermia and radiation for treatment of prostate cancer in 26 patients with stage T3 or N+ prostate cancer with median follow-up of 71 months. Similar to the Hurwitz trial, all patients received EBRT using a four-field technique. The median radiation dose was 68 Gy in 2 Gy fractions. The thermal treatment goal in this initial study was to obtain temperatures of 42.5°C within the prostate for 30 min for either one or two hyperthermia treatments. The disease-free survival rate was 39%. The median pretreatment prostate-specific antigen (PSA) level was 29 ng/ml (range, 6–104 ng/ml).

Another interstitial hyperthermia technique is multielectrode current source (MECS) interstitial hyperthermia. Adequate hyperthermia has proven difficult to achieve with regional radiofrequency technology.<sup>25</sup> Regional radiofrequency systems resulted in relatively low tumor temperatures during treatment.<sup>31</sup> The MECS interstitial hyperthermia system uses segmented radiofrequency electrodes. Each individual electrode controls the locally measured tissue temperature.<sup>32,33</sup>

As early as 1994, a phase I study was reported comprising 36 patients with prostate cancer (5 with locally recurrent, 15 with a T2, and 16 with T3 stage prostate cancer), treated with radiofrequency-induced hyperthermia and iridium-192 brachytherapy from 1987 until 1992.<sup>34</sup> In this study, two-dimensional, steered 0.5 MHz radiofrequency-induced interstitial hyperthermia was administered in combination with 50 Gy external radiation for 5 weeks, followed by 30 Gy iridium-192 interstitial brachytherapy. Two hyperthermia sessions for 45 min were planned, immediately before and after brachytherapy. Between 7 and 32 1.5 mm steel trocar hyperthermia electrodes were positioned transperineally in the prostate.

Van Vulpen et al<sup>35</sup> published a feasibility study of interstitial hyperthermia for prostate carcinoma using the MECS interstitial hyperthermia system on 12 patients with prostate cancer (T3NxM0), who were treated between July 1999 and January 2001. Conformal radiation therapy using a three-field technique with 6 and 18 MV photons delivered 70 Gy in 2 Gy fractions to the prostate and seminal vesicles. The average overall patient temperature measured on the heating catheters was 44.3°C. The bladder and rectal temperatures were below 40°C. The authors reported that an MECS interstitial hyperthermia treatment in combination with radiation was well tolerated. During the hyperthermia sessions, no side-effects occurred. In the combined treatments, no toxicity above grade 2 was seen for urinary, rectal, constitutional, and sexual complaints. In both publications<sup>34,35</sup> long-term survival data was not included.

An innovative therapeutic approach for the treatment of prostate cancer is interstitial hyperthermia in combination with percutaneous radiation therapy, using implantable ferromagnetic thermoseeds, which generate heat by induction in a magnetic field. Ferromagnetism is based on the quantum mechanical nature of the inner electrons of a material and leads to the generation of a dipole. At the so-called Curie temperature, the material loses its magnetic dipole momentum. Paramagnetism occurs when the temperature of the alloy rises above this value. If ferromagnetic material is exposed to a surrounding field, atomic dipoles straighten out, and, when the field oscillates, heat is generated. The material heats up until the Curie temperature is reached and the ferromagnetic characteristics are lost. The selection of alloys with a known Curie temperature allows for a self-regulating system. Based on these specifications, thermoseeds with a defined Curie point can be chosen.<sup>36-38</sup> Since the ferromagnetic implants remain in the prostate, hyperthermia induction can be repeated as often as necessary.

Several investigators have described animal models using ferromagnetic thermoseeds for prostate treatment.<sup>39-41</sup> Deger et al<sup>42</sup> used ferromagnetic cobalt-palladium alloy thermoseeds for interstitial hyperthermia in combination with ERBT for prostate cancer patients. This study group examined several alloys such as nickel-copper before evaluating the optimal biocompatibility. Cobalt-palladium was the most promising alloy,<sup>38,43,44</sup> while other investigators also reported on palladium-nickel and ferrite core/metallic sheath thermoseeds.<sup>45,46</sup>

To achieve interstitial hyperthermia, Deger et al<sup>42,47</sup> used thermoseeds with a Curie temperature of 55°C. They added a three-dimensional conformal radiotherapy of 68.4 Gy, given simultaneously with hyperthermia in daily fractions of 1.8 Gy. A patented coil system (50 kHz) was utilized to establish the magnetic field. Six 60-min hyperthermia treatments were conducted in all patients at an interval of 1 week. Using thermocouples,

the measured intraprostatic temperatures were found to be between 42°C and 48°C. During treatment the urethral and rectal temperatures were measured to be between 38°C and 43°C and between 37°C and 39.5°C, respectively.<sup>48</sup> No seed migration was observed on follow-up X-rays. At a mean follow-up time of 15 months, 5% (3/57) patients showed progression of disease at an average time of 20.3 months. Initial mean PSA value of these patients was 34 ng/ml; all had T3 disease. Two patients had local and 1 patient had systemic progression. PSA follow-up data of this patient group were comparable to the data of the patients treated with a high dose rate brachytherapy<sup>49</sup> and better than those of the patients who received conformal radiation therapy in the same institution.

Currently, the literature does not provide enough oncologic data on the use of hyperthermia for the treatment of prostate cancer. Most studies describe feasibility and toxicity. Nevertheless, interstitial hyperthermia in combination with conformal radiotherapy may be a powerful new method of improving the results of EBRT for localized prostate cancer. In addition, the combination of hyperthermia with chemotherapeutics<sup>50,51</sup> or thermo- or radiosensitizing modalities<sup>52-54</sup> may offer further potential in improving the treatment of localized prostate cancer with lower morbidity than current treatment options.

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## Hand-assisted laparoscopic nephrectomy

Steven J Shichman and Joseph R Wagner

Hand-assisted laparoscopic nephrectomy (HALN) was introduced in 1996 when Bannenberg et al performed the first nephrectomy in the pig.<sup>1</sup> They reported that the HALN technique was quick and easy to perform and, compared with conventional laparoscopic nephrectomy, operative times were shorter (30–45 min versus 90 to 120 min). In 1997 Nakada and colleagues reported the first HALN in a human for removal of a chronically infected kidney from stone disease.<sup>2</sup> Since 1997, numerous publications have reported the use of hand-assisted techniques for radical nephrectomies, nephroureterectomies, donor nephrectomies, partial nephrectomies, and dismembered pyeloplasties.<sup>3–7</sup> Since 1998, we have performed over 500 hand-assisted laparoscopic renal procedures using handassisted techniques.

Hand-assisted techniques utilize all the principles of standard laparoscopy, but offer surgeons the advantage of using their most versatile instrument—their hands. The hand aids in dissection, exposure, retraction, and maintaining hemostasis. The hand may also assist in more advanced techniques, such as intracorporeal suturing and knot tying. Furthermore, by maintaining tactile sensation, the surgeon is able to palpate vessels and organs that he may not be able to discern by visualization alone, thereby potentially minimizing the risk of injury to vital structures, particularly during difficult dissections. In essence, handassisted laparoscopy combines the advantages of laparoscopic and open surgery. As said by Dr RV Clayman, ‘one hand is worth a thousand trocars’.<sup>8</sup>

### Indications

Indications for HALN can include almost any scenario in which an open nephrectomy is warranted. The most common indications include nephrectomy for functional renal masses (renal cell carcinoma being the most common pathology), nonfunctioning kidneys, and renovascular hypertension. Hand-assisted techniques can also be applied to nephroureterectomy (hand-assisted laparoscopic nephroureterectomy, HALNU) for live donor renal transplants and upper tract transitional cell carcinoma.

Care must be taken in evaluating whether a patient is appropriate for HALN (Table 48.1). The most favorable patients, especially during the initial learning phase, include those who are relatively thin and have left-sided tumors. Patients with virgin abdominal cavities and small, lower pole tumors located away from the renal hilum are ideal candidates.

Several conditions make a patient less than ideal for initial attempts at hand-assisted cases. Obese patients can be a significant challenge, since excessive adipose tissue can make dissection tedious and difficult. Multiple prior abdominal surgeries predispose to intraperitoneal adhesions, which are time consuming to lyse and increase the risk of visceral injury. Patients with extremely muscular abdominal walls have reduced abdominal wall compliance, which reduces the working space and thereby restricts the use of the hand. Relative contraindications to hand-assisted techniques also include extremely large tumors, extensive renal vein or inferior vena cava (IVC) thrombus, history of severe perirenal and/or intra-abdominal inflammatory conditions, ipsilateral abdominal wall stomas, and pregnancy. As the surgeon's experience grows, patients with relative contraindications become more amenable to the hand-assisted technique. Absolute contraindications include caval thrombus extending above the hepatic veins, large tumors with direct extension into the body wall or adjacent viscera, and uncorrectable bleeding disorders.

### Hand-access devices

The purpose of the hand-access device is to enable the surgeon to comfortably insert his nondominant hand into the abdominal cavity through a small incision without the loss of the pneumoperitoneum.

There is no perfect hand-access device. Each device has its advantages and disadvantages. Factors determining the ideal choice of a hand-access device for a specific case

**Table 48.1** *Favourable aspects relative contraindications, and absolute contraindications to performing hand-assisted laproscopy nephrectomy*

| Favorable aspects                        | Relative contraindications               | Absolute contraindications                                   |
|--|--|--|
| Thin body habitus                        | Morbid obesity                           | Caval thrombus extending above hepatic veins                 |
| Small tumors                             | Severe intraperitoneal adhesions         |  |
| Left-sided tumors                        | Severe perirenal and perihilar adhesions | Direct extension of tumor into body wall or adjacent viscera |
| Lower pole tumors                        | Muscular abdominal wall                  |  |
| Tumors located away from the renal hilum | Extremely large tumors (>15 cm)          | Uncorrectable bleeding disorder                              |
| Minimal or no previous abdominal surgery | Extensive renal vein or IVC thrombus     |  |
|  | Ipsilateral abdominal wall stoma         |  |
|  | Pregnancy                                |  |
| IVC, inferior vena cava.                 |  |  |

include the patient's body habitus and pathology, and the surgeon's experience and preference using each individual device. All devices require a similar size incision (3–4 inches) in the abdominal wall, but vary widely on how they maintain a seal around the surgeon's arm and wrist. Unlike the first-generation devices, none of the new products

adheres to the body wall using adhesive seals. These adhesive seals were tedious and difficult to apply and were very prone to leakage.

Devices, which are currently on the market, include the following:

1. GelPort—Applied Medical Resources Corporation, Rancho Santa Margarita, California.
2. Lap Disc—Ethicon Endosurgery, Inc., Cincinnati, Ohio.
3. OmniPort—InterMed, Selling, Nevada
4. HandPort—Smith & Nephew, Largo, Florida, recently acquired by Ethicon Endosurgery, Inc., Cincinnati, Ohio.

All of these devices secure to the body wall using two concentric rings that are attached together with vinyl or rubber. One ring is inserted on the undersurface of the abdominal wall and the other ring rests on the outside surface of the body wall. The material holding the two rings together is placed on stretch, maintaining the seal at the body wall and acting as a wound protector. These second-generation devices can be directly inserted into the abdominal cavity without first insufflating, which is a definite time saver.

Advantages of the GelPort (Figure 48.1) device include an excellent seal, flexibility, and comfort offered by the gel. The unique gel-like polymer through which the surgeon inserts his hand is flexible and soft around the wrist. Additionally, this polymer can be temporarily pierced by an instrument or trocar and maintain a seal at the puncture site. Instruments can even be inserted through the gel while the hand is inserted in the device. Other advantages include the fact that removal of the surgeon's hand from the abdominal cavity does not cause loss of pneumoperitoneum and rarely causes the device to become dislodged. The GelPort device has the largest template or footprint, requiring a large area for application. This is not a problem in most cases, but in small-framed patients the device may be too large to use in a right lower quadrant incision that is commonly used for a right-sided nephrectomy. In these cases the anterior iliac spine may prevent the device from sitting evenly against the body wall, thereby jeopardizing the seal. A smaller version of this device has recently become available to obviate these problems. GelPort is the most expensive hand-access device on the market.

The Lap Disc (Figure 48.2) is the least expensive device on the market and is the easiest to use. There are no pieces



**Figure 48.1**

The GelPort device is made of a comfortable gel-like polymer which allows insertion of both hand and trocar



**Figure 48.2**

The Lap Disc device has an adjustable iris which can tighten around a surgeon's wrist or trocar to develop a seal. This is the least expensive hand-assist device on the market.

that need to be assembled, and insertion of the device is quick and easy. This device has the smallest footprint, fitting almost anywhere on most abdominal walls and rarely interferes with adjacent trocars. An oversized device is available for patients with thicker than normal abdominal walls. The iris that tightens around the surgeon's wrist, to develop the seal, can alternatively be tightened around a trocar or completely closed on itself to maintain the pneumoperitoneum. This iris requires meticulous adjustment around the wrist. If it is too tight, the hand will quickly tire and become painful; if too loose, the device will leak. When removing the hand from the abdomen the iris must be adequately loosened or the Lap Disc will inadvertently be removed. Pneumoperitoneum is lost when the hand is removed but can easily be re-established by quickly closing the iris.

The OmniPort (Figure 48.3) is an inflatable device, which maintains an excellent seal and rarely becomes dislodged once it is inserted. As with the GelPort and Lap Disc, the surgeon can rapidly remove and reinsert his hand, which is a major advantage for resident teaching programs when the teaching surgeon must quickly take over the case to avert or manage a potential complication. The device can be insufflated to maintain pneumoperitoneum without the hand



**Figure 48.3**

The OmniPort device maintains an excellent seal via an inflatable mechanism.

being inserted, but an accessory trocar or instrument cannot be inserted through the device. Unfortunately, the device can be difficult to insert. Additionally, care must be taken to ensure that the bowel or omentum is not caught under the rigid inner ring, which is unforgiving and can easily damage soft tissue.

The inflatable HandPort (Figure 48.4) is probably the most comfortable device, as there are no rigid pieces to rub against the wrist or forearm. Unfortunately, without a

rigid inner ring, the device can easily become dislodged. To develop a seal around the arm, the surgeon must wear a sleeve that attaches at the wrist and is covered by a second glove. This sleeve wedges the surgeon to the device and makes insertion or removal of the hand and switching surgeons more complicated and time consuming. Additionally, removal of the sleeve from the device does cause immediate loss of pneumoperitoneum. This device has an available insert that can be used to maintain pneumoperitoneum without insertion of the hand and can be used for insertion of an accessory trocar or instrument.

As with all forms of minimally invasive surgery, products will continue to change and improve. It is not practical or cost-effective for any one operating room to have all products available. Surgeons performing hand-assisted laparoscopy should periodically evaluate the hand-access devices available and select the one or two devices they feel are best suited for their needs.

### **Trocar and hand-port configuration**

We have used the following hand incision and trocar configurations successfully in over 500 cases with little modification. Numerous factors must be considered when determining the optimal positioning of trocars and the hand incision. These factors include the specific operation being performed, the patient's anatomy, the surgeon's experience, and the surgeon's hand and forearm size.

The patient is positioned in the semilateral decubitus position and secured to the table with 3 inch cloth tape across the shoulders, hips, and legs (Figure 48.5). At the start of the case, the table is rolled so that the patient is in a near-supine position. Placement of the hand incision is made with the patient in this position, as this allows for easier access to the peritoneal cavity and ensures better cosmetic results, especially in obese patients.

The midline should always be marked, which aids in trocar placement as well as provides a quick and accurate guide if emergent laparotomy is necessary. The use of 12 mm trocars in all port sites enables the camera and endoscopic stapler to be placed through any trocar to allow maximum flexibility. For a right-sided nephrectomy, a 5 mm trocar is used in the right upper quadrant for placement of a liver retractor, as a camera or stapler would never be used at this site.



**Figure 48.4**

The inflatable HandPort device does not have a rigid inner ring, making it very comfortable for the surgeon. However, the HandPort is easily dislodged.



**Figure 48.5**

Patient positioning for the hand-assist laparoscopic nephrectomy is the semi-lateral decubitus position.

The length of the hand incision in centimeters is usually equal to the surgeon's glove size. Once the incision is made and the peritoneal cavity is entered, test the size and length of the incision for comfort. If the incision is too small, paresthesias and cramping of the surgeon's hand can result, which will make the operation more difficult. Too large of an incision may result in the hand device becoming dislodged and loss of the pneumoperitoneum.

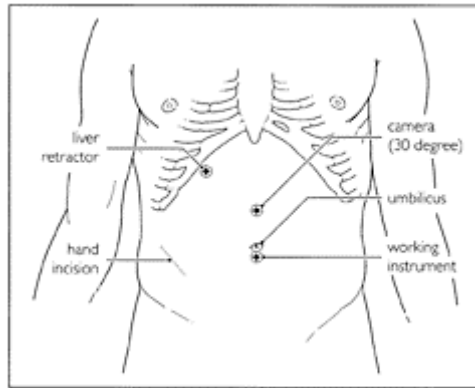
The renal hilum is approximately 8–12 cm superior to the umbilicus, but this distance can vary widely based on the patient's body habitus and vascular anatomy. Examine the patient's computed tomography (CT) scan and calculate this distance by counting the number of tomographic images between the renal hilum and the umbilicus. If the distance is greater than 12 cm, the surgeon has short arms, the patient is obese, or the girth of the abdominal cavity is larger than normal, consider moving the hand incision cephalad, which allows improved access to the renal hilum.

The hand incision should be at such a distance from the operative target as to allow insertion of the entire hand and wrist into the peritoneal cavity. The surgeon's wrist should have free range of motion and the fingertips should comfortably reach the renal hilum (the most important part of the dissection). If the hand incision is placed too close to the kidney, the hand will not be able to be completely inserted into the abdominal cavity, losing maneuverability of the wrist and fingers. The hand will act more as a retractor and less optimally as a dissector.

Attempt to place the hand incision as low as possible on the abdominal cavity, as this will result in decreased postoperative discomfort and respiratory compromise. Additionally, always try to avoid cutting muscle fibers, as this will reduce postoperative morbidity and reduce the risk of incisional hernias. We use a low midline or periumbilical hand incision for a left nephrectomy and a musclesplitting right lower quadrant incision for a right nephrectomy.

For a right-sided nephrectomy (Figure 48.6), the hand incision is placed in the right lower quadrant lateral to the rectus muscle, just below the level of the umbilicus. The skin is incised in line with the external oblique fascial fibers and the abdominal wall musculature is split. In a small percentage of right-sided cases, the incision is made in line with the internal oblique fibers and shifted more cephalad. This alteration gives the surgeon the option to extend the incision cephalad and medially, creating a low lateral subcostal incision if the case cannot be completed laparoscopically. One must keep in mind that if emergent conversion is required, an incision should be made in a location that will allow most efficient and safe management of the





**Figure 48.6**

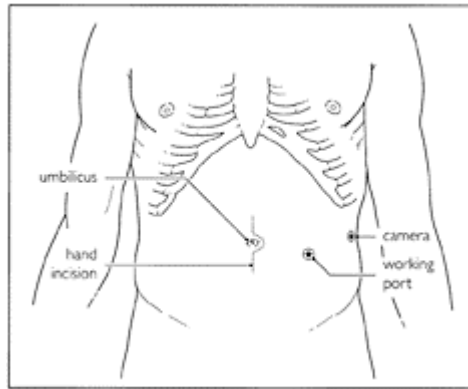
Trocar and hand-port placement: right. The hand-assisted device for right-sided nephrectomy is placed in the right lower quadrant lateral to the rectus muscle, just below the level of the umbilicus.

situation at hand. Do not try to manage a complication or difficult case through an extended hand incision if it will not offer optimal exposure.

After insertion of the hand-assist device, the working instrument port is placed just below or above the umbilicus and the camera port is placed in the supraumbilical midline, approximately 6–8 cm cephalad to the working trocar. The camera and working instruments may be switched at any time to facilitate the dissection. A third port is placed in the right midclavicular line at the costal margin, which allows placement of a liver retractor. Placement of this port more medially will result in the liver retractor leaning against the gallbladder, potentially causing injury.

For a left-sided nephrectomy (Figure 48.7), the hand port is placed midline in the infraumbilical or periumbilical region. The camera port is placed in the anterior axillary line at the level of the umbilicus while the working instrument port is placed in the midclavicular line, just below the level of the umbilicus. For very large upper pole tumors an additional superior midclavicular working port may be used for the most cephalad part of the dissection. Adequate mobilization of the spleen obviates the need for a splenic retraction port.

In morbidly obese patients or patients with very rotund and protuberant abdominal walls, the hand and trocar template is shifted lateral and cephalad. In a left-sided nephrectomy, the hand incision is placed lateral to the rectus muscle belly and the two trocar sites are moved approximately equidistance lateral to their standard locations. In a right-sided nephrectomy, the hand-access incision and trocar sites can be moved lateral any distance, as



**Figure 48.7**

Trocar and hand-port placement: left.  
The hand-assist device for left-sided  
nephrectomy is placed in the  
infraumbilical or periumbilical region.

the hand-access incision is already lateral to the rectus muscle belly.

In almost all cases we start out by making the hand incision and inserting the hand-access device and trocars prior to establishing a pneumoperitoneum. In cases where there is a high index of suspicion for significant adhesions, the hand incision allows direct visualization of the abdominal cavity and open surgical lysis of adhesions. Taking down extensive intra-abdominal adhesions through the hand incision can save a significant amount of time as compared to using a purely laparoscopic technique.

Another option is to initially establish the pneumoperitoneum using a Hasson trocar or Veress needle and inspect the peritoneal cavity using the laparoscope. This allows the surgeon to identify adhesions and appreciate variations of anatomy that may alter the positioning of the hand-assist device and/or trocars. We stopped using this technique after our first 100 cases as we found that the placement of our hand incision and trocar placement was rarely if ever modified.

Once the pneumoperitoneum is established, it is maintained at a pressure of 12–15 mmHg as per standard laparoscopy.

### **Stepwise dissection technique**

#### *Left radical nephrectomy*

The colon is released from the lateral sidewall by incising the white line of Toldt. Dissection is carried out from the splenic flexure to the iliac vessels. The colon is reflected medially using the back of the hand, while the fingertips help dissect the mesocolon off of the anterior aspect of Gerota's fascia. Dissection is continued in the

cephalad direction, freeing the splenic flexure and releasing the splenorenal ligaments. The lateral attachments from the body sidewall to the spleen are now released up to the level of the gastric fundus, which allows the entire spleen and splenic flexure to fall medially. Do not release the lateral attachments of the kidney to the body sidewall, as these attachments are used for countertraction, which aids in the medial dissection of the renal hilum. The plane between the tail of the pancreas and the anterior aspect of Gerota's fascia is then developed, which allows the tail of the pancreas to rotate medially with the spleen. The back of the hand is used as an atraumatic retractor on the spleen and the pancreas, while the fingertips aid in dissection. Care is taken to leave the entire anterior aspect of Gerota's fascia intact. The colon and mesocolon are mobilized medially to allow identification of the aorta and renal hilum. Investing tissue overlying the hilar vessels is grasped with the fingertips, retracted anteriorly, and a plane between these tissues and renal vein is developed using the harmonic scalpel or scissors. Once the anterior wall of the renal vein is exposed, meticulous dissection allows identification of both the gonadal vein and left adrenal vein entering the renal vein. These veins are dissected free of their surrounding tissues and doubly clipped both proximally and distally.

In some cases we choose not to clip and divide the gonadal and adrenal vessels at this point in the procedure, as we do not want to have clips potentially interfere with the subsequent firing of the linear stapling device across the renal vein later in the case. In other cases the anatomy may be favorable for dividing the renal vein proximal to the adrenal vein, obviating the need for division of the adrenal and gonadal veins as long as the surgeon plans on removal of the adrenal gland with the kidney.

At this point, the surgeon must not be tempted to continue dissection of the renal vasculature from this anterior approach. The key to the success of the HALN is obtaining the vascular control from a posterior approach, which allows the fingertips to surround the renal hilum, helping with palpation, dissection, and control of the renal artery and vein. In a very rare case the main renal artery will be easily accessible anteriorly and should obviously be ligated and divided at this point in the procedure.

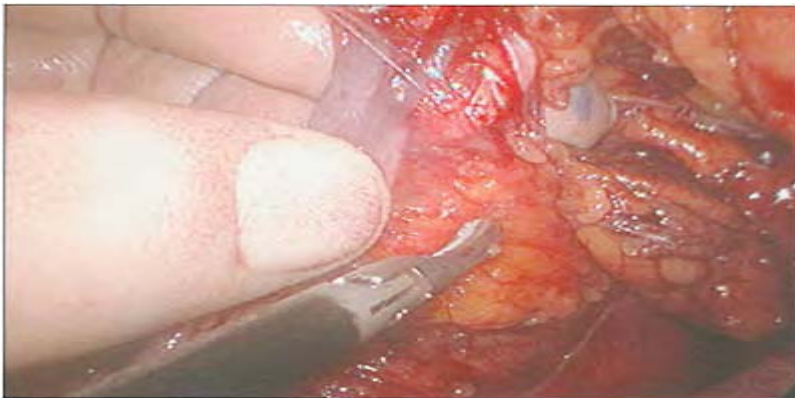
Dissection now continues at the most inferior lateral portion of Gerota's fascia, identifying the body sidewall and psoas muscle. The fingertips and the dissecting instrument of choice, either electrocautery scissors or harmonic scalpel, are used to reflect the perinephric fat in a medial and anterior direction off the psoas muscle. The surgeon works from a lateral to medial direction, coming across the gonadal vein, which is doubly clipped, proximally and distally with hemoclips and divided. If a radical nephrectomy is performed, the ureter is also identified, clipped and transected. Obviously, during a nephroureterectomy, the ureter is left intact. If a donor nephrectomy is being performed, the periureteral tissue is left adjacent to the ureter as well as leaving the ureter intact, and dissection of the ureter with all of its surrounding tissue is continued into the true pelvis below the iliac vessels.

The surgeon continues reflecting the inferior pole of the kidney, adjacent perinephric fat, and overlying Gerota's fascia anteriorly and medially, releasing the posterior and lateral attachments to the body sidewall and posterior wall. All lateral attachments are now released up to the level of the adrenal gland, as the kidney is reflected anteriorly and medially with the back of the hand. Care must be taken not to enter Gerota's fascia. As the lateral attachments to the inferior aspect of the diaphragm are encountered, the

surgeon must be careful not to perforate through the diaphragm. If perforation occurs, rapid loss of pneumoperitoneum will occur, resulting in a tension pneumothorax. Perforations can be closed using hand-assisted laparoscopic suturing techniques; conversion to open nephrectomy may be necessary.

After releasing all lateral and posterior attachments, the kidney can be rolled anteriorly and medially, exposing the posterior aspect of the renal pedicle. The kidney should then be rolled back to its normal position and the tips of the second and third finger are placed just above the exposed anterior aspect of the renal vein. Using the thumb and dissecting instrument, the kidney is now rolled anteriorly and medially and the thumb is placed on the posterior aspect of the renal vessels (Figure 48.8). This maneuver helps identify the renal artery by direct palpation and allows for presentation of the artery to the dissecting instruments. Additionally, if bleeding is encountered, the fingers can compress the pedicle, achieving rapid hemostasis. Using curved electrocautery shears, a Maryland dissector, or a harmonic scalpel to dissect the surrounding lymphatic tissue, the posterior and inferior aspects of the renal artery are exposed. Oftentimes, a lumbar vein is seen coursing across the posterior aspect of the proximal renal artery. This lumbar vein can complicate exposure and dissection of the renal hilum, as it may tether the renal vein or obscure the renal artery. In these situations, the lumbar vein must be clipped and divided. Following this, a rightangle dissector is passed around the renal artery, completely freeing the vessel from all remaining attachments. The artery can be controlled using either three locking clips, two proximally and one distally, or by using an endoscopic linear stapling device.

After the renal artery is divided, the renal vein is freed of all surrounding lymphatic and connective tissues, and controlled using an endoscopic linear stapling device or large hemoclips. When the endoscopic stapler is used, great care must be taken not to engage any previously placed



**Figure 48.8**

The left renal artery is localized by rolling the kidney anteriorly and medially and placing the thumb on the

posterior aspect of the renal hilum.  
With bimanual palpation, the artery  
can be localized and dissected free of  
lymphatic tissue.

clips in between the jaws of the stapler. Both visual inspection and palpation with the hand ensures that the stapler has not engaged any extraneous tissue or clips. Engaging clips in the jaws of the stapler will cause the device to misfire, resulting in a disruption of the staple line and significant bleeding.

If the adrenal gland needs to be removed with the left kidney, attention is now directed to the most superior phrenic attachments. With the spleen completely mobilized medially, diaphragmatic attachments are identified and controlled using hemoclips or the harmonic scalpel. There is usually a single artery originating from the diaphragmatic attachment, which must be clipped for adequate control. The remaining vessels can usually be divided using the harmonic scalpel. Care must be taken to identify any accessory phrenic veins that may exist, coursing from the diaphragm along the medial aspect of the adrenal gland toward the renal vein. These structures can be easily mistaken for the adrenal vein when dissecting in the region of the superior aspect of the renal vein. The superolateral attachments from the adrenal gland to the body sidewall are left intact and the medial attachments to the aorta are divided using the harmonic scalpel and clips when necessary. The remaining superolateral attachments and posterior attachments are now divided using the harmonic scalpel or electrocautery scissors and the specimen is completely freed.

If the adrenal gland is to be left intact, use visual inspection and palpation with the fingertips to locate the groove separating the adrenal gland from the kidney. The attachments between the adrenal gland and the superior aspect of the kidney are divided using the harmonic scalpel. If the adrenal vein has not already been divided, it should be doubly clipped proximally and distally, and sharply transected. Usually, a single large arterial branch originating from the renal artery feeds the most inferior lateral aspect of the adrenal gland. Hemoclips can be used on this vessel for adequate hemostasis.

Once dissection is complete, the kidney is removed through the hand incision. Oncologic principles are no different in the hand-assisted technique than in that of open surgery. The specimen is delivered intact, without the need for morcellation, preserving the pathologic integrity of the specimen. The hand is placed back into the abdomen and pneumoperitoneum is re-established. Adequate hemostasis should be ensured at lower insufflation pressures (5–8 mmHg), confirming vascular control of all arterial and venous structures. Renal hilar vascular stumps are re-examined and any bleeding staple lines or vascular stumps can be controlled with laparoscopic suture ligation.

### *Right radical nephrectomy*

After insertion of the hand device and trocars as previously described, the liver retractor is inserted and the liver is retracted medially. The right lobe of the liver is released from the body sidewall by incising the triangular ligament and, if necessary, the anterior and posterior divisions of the coronary ligaments. There may also be significant attachments between the undersurface of the right lobe of the liver and the anterior/superior aspect of Gerota's fascia that must be released using the harmonic scalpel.

With the liver adequately mobilized medially, the attachments of the hepatic flexure to the overlying Gerota's fascia are released using the fingertips to develop pedicles, which are transected using the harmonic scalpel. The duodenum is now identified. If the vena cava is covered by the duodenum at the level of the renal hilum, a standard Kocher maneuver is performed using sharp dissection, mobilizing the duodenum medially off of the underlying renal hilum and vena cava. Investing tissue over the vena cava and renal vein is released and the anterior wall of the renal vein is skeletonized. The tendency will be to continue dissection on the renal hilum and vasculature at this time, but the surgeon should remember it is imperative to obtain vascular control from the posterior approach.

Posterior exposure of the renal hilum is obtained by releasing all attachments of Gerota's fascia and perinephric fat to the body wall and rotating the kidney anteriorly and medially. We start this part of the dissection by directing our attention to the perinephric fat inferior to the lower pole of the kidney. Using fingertip dissection, the psoas muscle is identified and the fingers are passed lateral to medial, raising the most caudal attachments of the kidney off of the psoas muscle. This large pedicle of tissue may include the right gonadal vein and ureter. The entire pedicle can be divided using an endoscopic linear stapling device. Alternatively, individual pedicles of fat can be divided using the harmonic scalpel, while the gonadal vein and ureter are individually clipped and sharply divided. In some cases the gonadal vein can be gently retracted medially and division of the vein is unnecessary. Attachments of Gerota's fascia and perinephric fat to the lateral and posterior body sidewall are released using the harmonic scalpel or electrocautery shears.

With the hand placed posterior to the kidney, the kidney is elevated. Any remaining inferior medial attachments to the vena cava or lower pole accessory veins are identified and secured using clips or the harmonic scalpel. The second and third fingers are now curled behind the renal pedicle, allowing identification of the renal artery (Figure 48.9). Using gentle traction with the index finger, the artery can be pulled inferiorly and dissected free of surrounding lymphatic tissue using the harmonic scalpel, Maryland dissector, or right-angle dissector. The artery can be controlled using locking clips or an endoscopic stapling device with a vascular cartridge. The renal vein is dissected free from surrounding lymphatic and investing tissues and transected using the endoscopic stapling device.

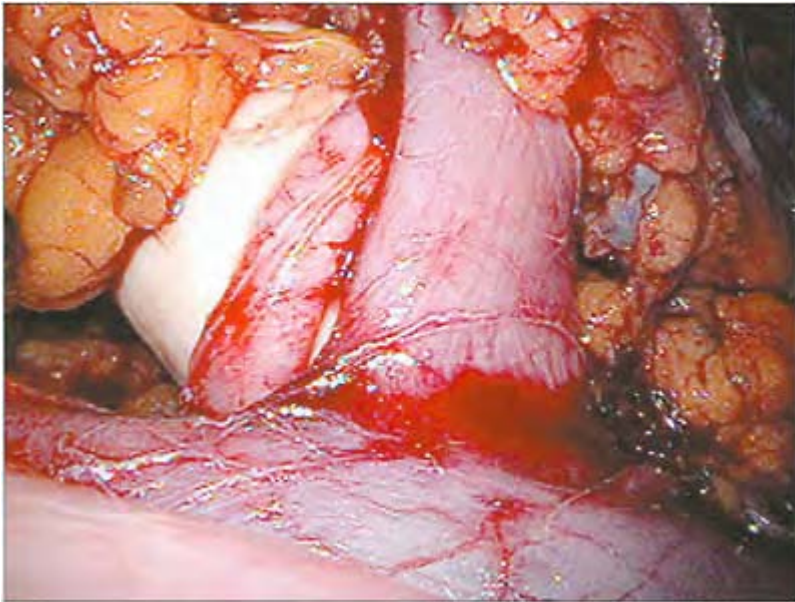
If the adrenal gland needs to be removed with the kidney, the liver must be aggressively mobilized medially. The most superior phrenic attachments and vessels feeding the adrenal gland should now be controlled and ligated with clips or the harmonic scalpel. The superolateral attachments should be left intact and dissection should continue along the vena cava, releasing medial attachments. The adrenal vein will now be easily identified and should be ligated using large hemoclips and sharply divided. The remaining posterior and lateral attachments can easily be transected using the harmonic scalpel.

If the adrenal gland does not need to be removed, use visual inspection and palpation with the fingertips to locate the groove separating the adrenal gland from the kidney. The attachments are divided using the harmonic scalpel.

### Comparison of open, laparoscopic, and hand-assisted renal surgery

Since the first laparoscopic nephrectomy was reported in 1991, the urologic community has increasingly accepted laparoscopic approaches for many urologic conditions.<sup>9</sup> This acceptance has been fostered by numerous articles demonstrating certain advantages to laparoscopic surgery, particularly decreased postoperative pain and a quicker recovery time to normal activity. In examining whether a new surgical technique is appropriate, one must address the technique's outcomes, morbidities, and costs. Many factors may affect more than one of these criteria: e.g. operative times may affect both morbidity and cost. If outcome, morbidity, and cost results are acceptable, one must then determine whether the new technique is transferable to other surgeons and institutions. Although such comparisons of different procedures are often difficult to interpret, certain trends are apparent when one examines open, laparoscopy, and hand-assisted laparoscopic (HAL) renal surgery.

For a purely ablative procedure, results demonstrate laparoscopic and HAL approaches are as efficacious as



**Figure 48.9** Localization of the right renal artery by placing the second and third fingers behind the renal pedicle. Utilizing gentle inferior retraction with the index finger, the artery is freed

from its surrounding lymphatic tissue  
with the harmonic scalpel.

open surgery. With 5 year follow-up, Portis et al demonstrated equal oncologic effectiveness for open and laparoscopic radical nephrectomy.<sup>10</sup> This had also been similarly demonstrated by Ono et al in 2001 for renal masses less than 5 cm.<sup>11</sup> Two-year follow-up data for laparoscopic and HAL nephroureterectomy is also encouraging.<sup>4,12</sup> However, long-term (>5 years) oncology outcomes are not available for HAL radical nephrectomy.

Laparoscopic partial nephrectomy can be daunting because of the potential for large blood loss and the need for reconstruction, which can be difficult. However, the laparoscopic procedure has been shown to have good pathologic outcomes, and HAL potentially facilitates hemostasis and suturing.<sup>13,14</sup>

Numerous studies have demonstrated equivalent graft function for open, laparoscopic, and HAL donor nephrectomy.<sup>15,16</sup> A randomized trial of HAL vs open donor nephrectomy clearly demonstrated less analgesic use, shorter hospital stay, and quicker return to normal activity in the HAL group.<sup>17</sup> Similarly, shorter hospital stays and quicker returns to normal activity were seen when HAL radical nephrectomy was compared to open radical nephrectomy.<sup>18</sup> Postoperative complications were similar across all groups in each of these studies. Numerous other studies have similarly shown quicker recoveries for HAL compared to open surgery. The biggest area of controversy is currently whether laparoscopic nephrectomy, particularly with morcellation, offers improved convalescence compared to HAL. Several studies suggest this is not the case.

Despite larger tumors in the HAL group, a nonrandomized study by Nelson and Wolf demonstrated equal recovery and morbidity in the HAL and morcellated laparoscopic groups.<sup>19</sup> A comparison of open, laparoscopic, and HAL donor nephrectomy showed equally shorter recovery times with laparoscopic and HAL nephrectomy.<sup>16</sup> During laparoscopic nephrectomy, no differences are seen in postoperative pain or hospital stay, whether a specimen is morcellated or removed intact.<sup>20</sup> Thus, HAL and laparoscopic renal surgery appear to be equivalent when examining postoperative recovery.

Cost analysis, while important, is a very difficult issue to address. Some studies have demonstrated increased costs associated with laparoscopic procedures due to instrument costs, whereas other studies have shown decreased costs due to decreased hospital stays.<sup>21,22</sup> The issue becomes even more confusing once physician time, patient work hours lost/gained, etc. are entered into the equation. Each element in the process (patient, surgeon, institution, etc.) will have a different cost/benefit ratio that should be considered, although absolute values will always be lacking.

While HAL and laparoscopic renal surgery show similar benefits, HAL is a more easily mastered technique and can be utilized in situations where laparoscopy alone may not be sufficient. Overcoming the lack of three-dimensional viewing is very difficult for the novice laparoscopist; HAL allows the surgeon's hand to be in the operative field and can compensate for the two-dimensional view. Open surgeons are not accustomed to operating with the long instruments and fulcrum points needed for laparoscopy; surgeons are comfortable dissecting and retracting with their open hand. HAL can also be helpful for large renal tumors that might not be as easily removed with straight laparoscopy. We have removed tumors up to 22 cm with HAL and feel nephrectomy under these



conditions is more easily performed with HAL than laparoscopy. Together, these factors describe a technique that is more easily learned and can be more widely applied than standard laparoscopy.

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## Laparoscopic surgery of the adrenal gland

David S Wang, Blake D Hamilton, and Howard N Winfield

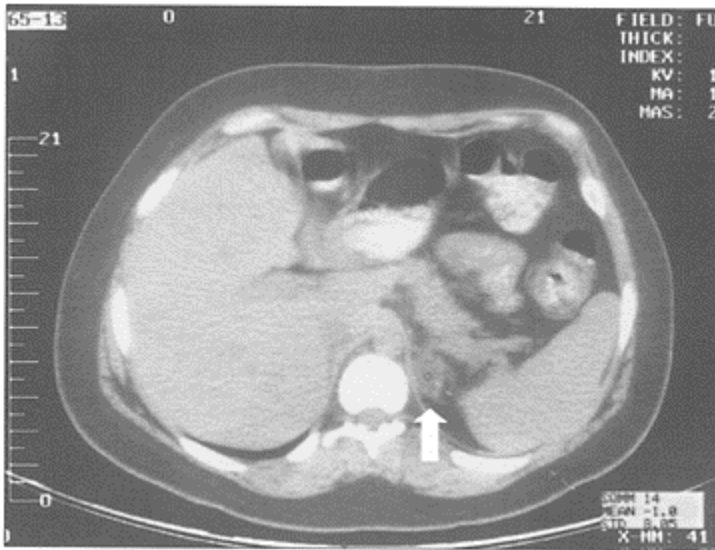
Since being first reported by Gagner et al. in 1992,<sup>1</sup> laparoscopic adrenalectomy has become an established procedure. Several comparative studies<sup>2-9</sup> have demonstrated the advantages of the laparoscopic approach to include decreased blood loss, less postoperative pain, shorter hospitalization, faster convalescence, and even cost-effectiveness.<sup>10</sup> As experience with laparoscopic adrenalectomy has been increasing, the indications for this procedure have expanded while the absolute contraindications for its use have diminished. Indeed, laparoscopic adrenalectomy has become a standard of care and the technique of choice for most benign adrenal lesions.

This chapter reviews the preoperative considerations, indications, technique, complications, and results of laparoscopic adrenalectomy.

### Diagnosis

Historically, adrenal lesions were diagnosed secondary to clinical manifestations of endocrinopathies. However, widespread use of abdominal ultrasound, computed tomography (CT) scans, and magnetic resonance imaging (MRI) has led to the rather frequent finding of the incidental adrenal mass. Figures 49.1 and 49.2 show typical examples of adrenal lesions diagnosed on CT and MRI, respectively. The differential diagnosis of the incidental adrenal mass is wide and includes the benign nonfunctioning adenoma, hormonally active cortical tumor, myelolipoma, pheochromocytoma, adrenocortical carcinoma, and metastatic lesion.

Tumors diagnosed incidentally on CT scans or MRI are managed according to size and hormone functional status.



**Figure 49.1** CT scan of the abdomen demonstrating left adrenal lesion (arrow).



**Figure 49.2** MRI of the abdomen demonstrating left adrenal lesion (arrow).

Patients with hormonally active adrenal tumors, such as aldosteronoma, Cushing's syndrome, or pheochromocytoma, should generally undergo surgical removal. Hormonal evaluation of these patients is critical because pre- and postoperative considerations regarding hypertensive control, electrolyte imbalances, and fluid shifts are paramount to ensure good surgical outcomes and minimize complications. A summary of standard laboratory tests in the evaluation of an adrenal lesion is listed in Table 49.1. Most hormonally active tumors should be removed, particularly in the case of pheochromocytoma and cortisol-secreting tumors.<sup>11,12</sup> Occasionally, medical management of aldosteronomas may be satisfactory to circumvent the need for surgical management, particularly in patients who are poor surgical candidates.<sup>13</sup> However side-effects of pharmacotherapy may become intolerable.

Hormonally inactive tumors have traditionally been managed according to size. Tumors less than 3 cm in size are almost always benign adenomas and generally require no further treatment unless clinical signs of hormonal activity develop. Tumors greater than 6 cm in size are worrisome for adrenocortical carcinomas, and thus surgical excision is recommended given the aggressive nature of adrenal cancer.<sup>14</sup> Nonfunctional lesions between 3 and 6 cm in size generally require close follow-up with serial imaging studies every 6 months. These lesions should be removed if tumors demonstrate interval change in appearance or develop endocrine activity.

As mentioned previously, lesions of the adrenal gland greater than 6 cm in size are worrisome for adrenal cancer. In one meta-analysis, 105 of 114 adrenocortical carcinomas measured 6 cm or greater in diameter.<sup>15</sup> Because a CT scan can underestimate the size of lesions by as much as 1 cm,<sup>16</sup> it is suggested that all lesions on CT scan which

**Table 49.1** *Routine laboratory tests useful in the evaluation of adrenal lesions*

*Cushing's syndrome*

- 24-hour urine cortisol
- Plasma ACTH and plasma cortisol
- Low-dose dexamethasone suppression test
- High-dose dexamethasone suppression test
- Metapyrone stimulation test
- Petrosal sinus ACTH measurement

*Hyperaldosteronism*

- Unprovoked hypokalemia
- Plasma aldosterone level
- Urinary aldosterone level
- Aldosterone-to-renin ratio
- Postural stimulation test
- Adrenal vein sampling of aldosterone

*Pheochromocytoma*

- Plasma catecholamines
- Urine catecholamines
- Clonidine suppression test
- Adrenal vein sampling of catecholamines

ACTH, adrenocorticotrophic hormone.

are 5 cm or greater in size be removed. In cases when there is concern for adrenal carcinoma with local extension into adjacent organs such as the kidney, colon, or spleen, open radical adrenalectomy with possible en bloc resection of adjacent organs is the preferred approach.<sup>17,18</sup> More recently, improvements in radiologic imaging techniques such as unenhanced CT with densitometry, delayed enhanced CT with densitometry, chemical-shift MRI, and NP-59 scintigraphy have further assisted in differentiating benign from malignant neoplasms.<sup>19</sup>

### **Indications for laparoscopic adrenalectomy**

The indications for laparoscopic adrenalectomy have expanded as more surgeons have become proficient with the technique and the advantages of this approach have become apparent. Laparoscopic adrenalectomy has in many centers become the surgical procedure of choice for the management of functional tumors less than 6 cm in size. Although the presence of pheochromocytoma was a relative contraindication for laparoscopic adrenalectomy in the past, it is clear that the procedure can be performed safely as long as the same precautions are taken as those for open surgery.<sup>20</sup> The current indications for performing a laparoscopic adrenalectomy are listed in Table 49.2.

There are very few absolute contraindications to laparoscopic adrenalectomy. It is generally felt that a known or suspected primary adrenal carcinoma, particularly with extension into surrounding organs, should be removed by an open technique. Given the aggressive nature of the disease, the open approach allows for en bloc resection and potential removal of surrounding organs.<sup>17</sup> The 5-year survival of completely vs incompletely resected primary adrenocortical carcinoma is 55% vs 5%,<sup>21</sup> respectively. The potential for surgical cure or improved survival should not be compromised for the sake of decreasing patient morbidity. Other contraindications to laparoscopic adrenalectomy include uncorrectable coagulopathy and cardiopulmonary disease precluding general anesthesia. Patients who will not tolerate an open operation are generally poor candidates for laparoscopic adrenalectomy.

Relative contraindications to laparoscopic adrenalectomy include previous abdominal surgery or significant morbidity. Lesions greater than 8 cm in size, even if not suspected to be primary adrenal carcinomas, should be approached cautiously because of the increased risk of hemorrhage and injury to surrounding viscera. With increasing experience in performing laparoscopic adrenalectomy, relative contraindications become less of a factor. In addition, a variety of approaches to laparoscopic adrenalectomy, including transperitoneal and retroperitoneal, have further decreased some of the relative contraindications.

Occasionally, the urologist will encounter a patient with a suspected solitary metastatic lesion to the adrenal gland. If the lesion is less than 6 cm in size and not obviously adherent to surrounding viscera, a laparoscopic approach is reasonable.<sup>22</sup> The surgeon should be already skilled in laparoscopic adrenalectomy before attempting to remove a solitary metastatic lesion given the more difficult surgical planes that are often present.

## Preoperative patient evaluation and preparation

Careful preoperative control and management of hormonally active tumors is critical prior to performing adrenal surgery, whether laparoscopic or open. Inadequate preoperative control of hormonally active lesions can lead to catastrophic intraoperative consequences. Close collaboration with an endocrinologist and anesthesiologist experienced with adrenal disorders is helpful. The urologist should have an understanding of the physiology of adrenal disorders in order to appropriately manage patients in the peri- and postoperative period with regard to fluid management, electrolyte abnormalities, and blood pressure control. Hormonally functional tumors must be adequately

### Table 49.2 *Indications for laproscopic adrenalectomy*

- Adlosterone-secreting adrenal gland, adenoma, or unilateral hyperplasia
- Cushing's syndrome secondary to adrenocortical adenoma
- Nonfunctional adrenal mass  $\leq 8$  cm with negative metastatic work-up
- Nonfunctional adrenal mass  $\leq 8$  cm with progressive growth on CT or MRI
- Adrenal pheochromocytoma (benign)  $\leq 8$  cm
- Solitary adrenal gland metastasis

evaluated and appropriate preoperative interventions initiated in concert with an endocrinologist.

Preoperatively, all patients should receive a mechanical bowel preparation. Clear liquids should be started the day before surgery. A broad-spectrum antibiotic should be administered on call to the operating room.

### *Aldosteronomas*

Primary hyperaldosteronism (Conn's syndrome) is a rare etiology of hypertension (less than 1%). Other clinical manifestations of Conn's syndrome arise from increased total body sodium content and a deficit in total body potassium. Symptoms include lower urinary tract symptoms, muscle weakness, paresthesias, or visual disturbances.<sup>13,23</sup> CT scan or MRI can detect adrenal adenomas as small as 1 cm. Laboratory manifestations include hypokalemia, elevated plasma and urinary aldosterone level, elevated serum aldosterone-to-renin ratio, and suppressed plasma renin activity.<sup>13,23</sup> Once an important part of the evaluation, adrenal vein sampling is now occasionally used to confirm and localize the lesion.

Once the diagnosis is confirmed, medical control of hypertension and correction of hypokalemia should be instituted at least several weeks prior to adrenalectomy. The most effective medication for management of hyperaldosteronism is spironolactone, a competitive antagonist of the aldosterone receptor.<sup>13</sup> Side-effects of spironolactone include hyperkalemia, sexual dysfunction, gynecomastia, gastrointestinal disturbances, and metabolic acidosis.<sup>24</sup> Alternative medications include potassium-sparing diuretics, calcium channel blockers, and converting enzyme inhibitors.<sup>23</sup> Hypertension is improved or cured in more than 90% of patients following adrenalectomy.<sup>25</sup>

*Cushing's syndrome*

Cushing's syndrome is used to describe the symptom complex that results from excess circulating glucocorticoids, regardless of etiology.<sup>12</sup> Nonadrenal causes of hypercortisolism include pituitary adenomas, ectopic corticotropin production, and exogenous steroid use. The urologist is most often confronted with an adrenal lesion as the etiology of Cushing's syndrome.

Cushing's syndrome manifests with a variety of wellrecognized clinical features, including hypertension, truncal obesity, moon facies, easy bruising, and mood disorders. Diagnosis is confirmed by laboratory testing.<sup>12</sup> Hypercortisolism is best diagnosed by 24-hour urinary cortisol measurement. The low-dose dexamethasone suppression test can be used to further diagnose Cushing's syndrome if urinary cortisol measurement is equivocal. Abdominal CT scan and MRI are used to identify adrenal adenomas or bilateral adrenal hyperplasia.

Adrenal adenomas causing Cushing's syndrome are very amenable to laparoscopic adrenalectomy. Open adrenal surgery is associated with significant perioperative morbidity, which results from the sequelae of chronic hypercortisolism. This presents as compromised wound healing, higher infection rate, diabetes, and increased risk of cardiopulmonary complications.

*Pheochromocytoma*

Pheochromocytomas can be challenging tumors to treat because of the unique manifestations of chronic and acute catecholamine excess. Once considered a relative contraindication to laparoscopic surgery, laparoscopic adrenalectomy for pheochromocytomas has now been performed successfully and reported in several series.<sup>20,26,27</sup> Successful laparoscopic adrenalectomy for pheochromocytoma involves close collaboration with the surgeon, endocrinologist, and anesthesiologist. Catecholamine excess results in hypertension, tachycardia, and a host of clinical manifestations. Laboratory diagnosis is made by elevated levels of catecholamines in the blood and urine. Radiographic diagnosis is achieved with either CT scan or MRI. MRI imaging classically demonstrates a bright image on a T2-weighted study.

Preoperative medical preparation includes optimal control of blood pressure with alpha blockade or calcium channel antagonists.<sup>11</sup> Beta-blockers may be used to control reflex tachycardia after initiation of the alpha blockade. In addition, aggressive fluid expansion is necessary to increase circulating plasma volume and prevent postoperative hypotension. Close monitoring intraoperatively includes careful attention to blood pressure, central venous pressure, and urinary output. An arterial line and central venous line are routinely used, and occasionally a Swan-Ganz catheter is employed. Severe hypertension can be controlled with sodium nitroprusside or phentolamine, and hypotension controlled with fluid resuscitation and norepinephrine.

**Surgical technique**

Perhaps no other urologic laparoscopic procedure has as many different surgical approaches as does adrenalectomy. Commonly used approaches to the adrenal gland

include the transperitoneal approaches, and the posterior and lateral retroperitoneal approaches. Recently, a transthoracic approach has been described for patients who have undergone extensive previous transperitoneal and retroperitoneal surgery.<sup>28</sup> Surgeon preference and experience appear to be the most important factors in determining the approach. Most surgeons are familiar with the anterior transperitoneal approach, but many who have overcome the learning curve of the anterior transperitoneal approach are becoming skilled with the retroperitoneal approach.<sup>29–34</sup> Although each approach has purported advantages and disadvantages, there is no clear-cut evidence that one is superior.<sup>35,36</sup>

### *Laparoscopic surgical anatomy*

A thorough knowledge of the anatomy of the adrenal gland and its relationship to adjacent organs is essential to avoid intraoperative complications. Familiarity with the vascular supply of the adrenal gland is important in minimizing the chances of intraoperative hemorrhage. The adrenal gland, like the kidney, is enveloped by Gerota's fascia; it is, however, located in a distinct fascial compartment that is separate from the kidney. The arterial supply to the adrenal gland arises from the inferior phrenic artery, aorta, and renal artery. A complex arcade of small arteries enters the adrenal gland from the medial and superior border of the gland, and thus the anterior, posterior, and inferolateral surfaces of the adrenal gland are relatively avascular.

The right and left adrenal gland have key anatomic differences in location and vasculature. The main right adrenal vein exits the gland from the superomedial surface and enters the inferior vena cava (IVC) directly. The longer left main adrenal vein exits the inferomedial aspect of the gland and drains into the left renal vein at an oblique angle. The right adrenal gland is more intimately related to the IVC than the left gland is related to the aorta. The capsule surrounding the adrenal gland is very fragile, and direct grasping of the adrenal gland can lead to parenchymal fracture resulting in persistent and troublesome bleeding. The lymphatic drainage of the adrenal gland includes all lateral aortic lymph node tissue between the diaphragm and ipsilateral renal artery. Regional lymphadenectomy is thus very challenging to perform laparoscopically.

### *Anterior transperitoneal approach for right adrenalectomy*

After general anesthesia by agents other than nitrous oxide, the patient is positioned with the right side elevated 45–70° upward and the table slightly flexed at the level of the umbilicus. The patient should be positioned on a beanbag with extensive padding over pressure points. Figure 49.3





**Figure 49.3** Patient positioning for right transperitoneal adrenalectomy.

shows the general modified flank position used for laparoscopic adrenalectomy. Next, the patient should be secured with tape to allow the table to be tilted side to side to facilitate exposure. A catheter is placed to drain the bladder, and an orogastric tube to decompress the stomach.

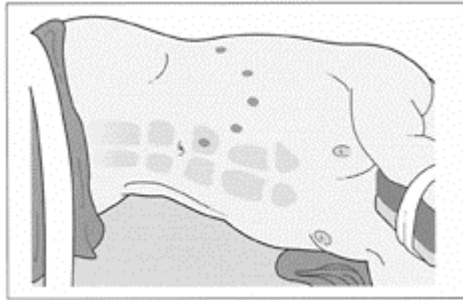
For a right laparoscopic adrenalectomy, four subcostal ports are used and placed two to three fingerbreadths below the costal margin, as depicted in Figure 49.4. Initial entry into the peritoneal cavity is made using the Veress needle just below the costal margin in the midclavicular line. Three additional ports are placed under direct vision; the most medial port is important for upward and medial retraction of the right lobe of the liver. Exposure of the right adrenal gland is dependent upon adequate mobilization of the liver.

Mobilization of the liver is the first step in exposing the right adrenal gland. Unlike laparoscopic nephrectomy, full mobilization of the ascending colon and hepatic flexure is unnecessary. Incision of the posterior peritoneum and extension through the triangular ligaments of the liver allow for upward and medial retraction of the liver (Figure 49.5).

The IVC is eventually identified once there is adequate liver mobilization. Continued and careful dissection along the lateral surface of the IVC will reveal the right adrenal vein (Figure 49.6). The adrenal vein should then be divided between standard clips. Dissection is further continued towards the diaphragm, and the inferior phrenic vessels should next be identified and divided.

The inferior pedicle of the adrenal gland is then released, separating the adrenal gland from the upper pole of the kidney. Gerota's fascia is next incised at the junction of the upper pole of the kidney and the adrenal gland. There is often an arterial branch to the

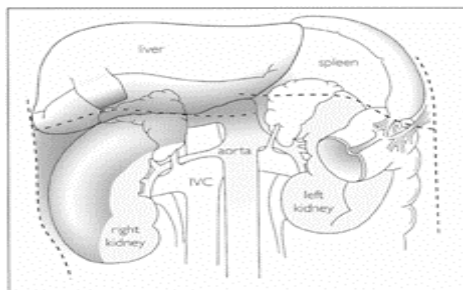
adrenal gland arising from the renal pedicle. Once the kidney is completely mobilized away from the adrenal gland, all that



**Figure 49.4** Trocar placement for a right transperitoneal adrenalectomy. An umbilical trocar is used for the camera. Other trocars are placed at the anterior axillary line and mid axillary line and are used for resection of the right adrenal gland. A fourth trocar is placed between the midline and anterior axillary line and is used for retraction of the liver.

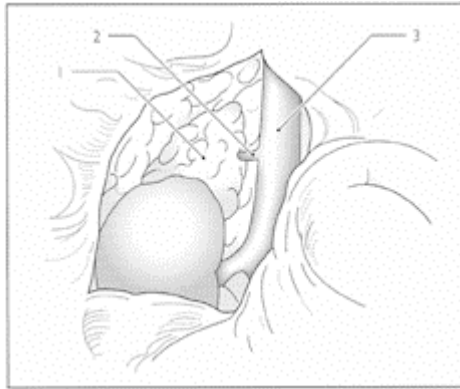
remains holding the adrenal gland in place is the relatively avascular lateral attachments, which are divided. Use of the harmonic scalpel can facilitate mobilization of the adrenal gland once the main vascular pedicles have been ligated.

Once the adrenal gland is completely separated, it should be placed in a specimen retrieval bag and removed en bloc. Assuming adequate hemostasis, the laparoscopic



**Figure 49.5** T-shaped incision through the posterior peritoneum for left and

right adrenalectomy. On the right, incision from second part of the duodenum to triangular ligaments at liver edge and then lateral to hepatic flexure. On the left, incision developed across phrenocolic and splenocolic ligaments and at the inferior border of the spleen. IVC=inferior vena cava.



**Figure 49.6** Dissection of the right adrenal gland (1). The right adrenal vein (2) is identified with careful dissection along the lateral surface of the inferior vena cava (3).

ports are removed under direct vision and the fascia closed with the Carter-Thomason fascial closure device. A drain is usually not necessary. The orogastric tube is removed at the conclusion of the procedure.

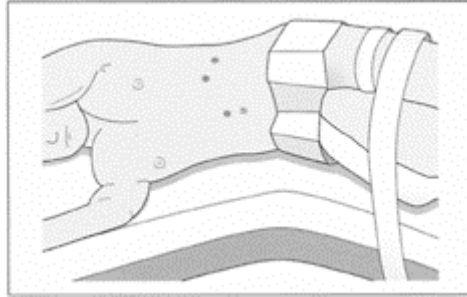
#### *Anterior transperitoneal approach for left adrenalectomy*

The patient is positioned with the left side elevated 45–70°, with the table slightly flexed at the level of the umbilicus (Figure 49.7). Three or four trocars are placed in a mirror image as for a right adrenalectomy. The important surrounding structures to identify when performing a transperitoneal left laparoscopic adrenalectomy are the spleen, the tail of the pancreas, the splenic flexure of the colon, and the left kidney. Full mobilization of the splenic flexure of the colon is necessary to provide adequate exposure to the left adrenal gland.

The first step after diagnostic laparoscopy is to incise the posterior peritoneum along the line of Toldt and mobilize the splenic flexure of the colon to allow the colon to fall

medially. The splenocolic and lienorenal ligaments are then mobilized to allow the spleen to be safely separated from the field of dissection (see Figure 49.5). This creates an adequate plane between the spleen and the upper pole of the left kidney. If necessary, the tail of the pancreas can be separated away from Gerota's fascia to allow the pancreas to fall away with the spleen to provide more exposure.

Next, Gerota's fascia is incised between the upper pole of the left kidney and the adrenal gland. The left adrenal gland should not be grasped directly, to avoid adrenal

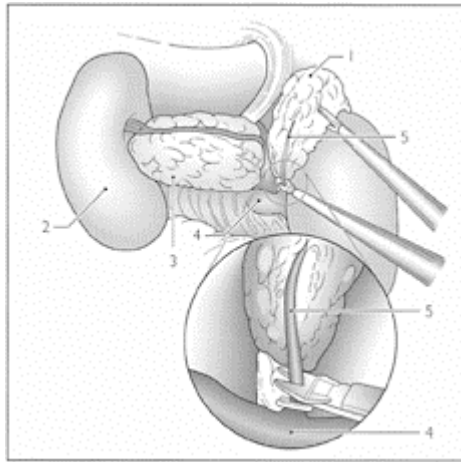


**Figure 49.7** Trocar placement for left transperitoneal adrenalectomy. An umbilical trocar is used for the camera. Other trocars are placed at the anterior axillary line and mid axillary line and are used for resection of the left adrenal gland. A fourth trocar is placed between the midline and anterior axillary line and is used for retraction of the spleen.

gland fractures, which are associated with troublesome bleeding. Dissection continues through the perirenal fibrofatty tissue. The inferior border of the adrenal gland is defined and the dissection continued medially. Medial dissection will eventually lead to the takeoff of the left adrenal vein emanating directly from the left renal vein. The left adrenal vein is then isolated, clipped, and divided (Figure 49.8). In the case of a pheochromocytoma, early exposure and ligation of the left adrenal vein is ideal to reduce the risk of a hypertensive crisis. We have found it easiest to initially identify the left renal vein and determine the takeoff of the left adrenal vein. Clipping of the adrenal vein at this juncture minimizes catecholamine surges.

The lateral attachments of the left adrenal gland should be saved until the remainder of the gland is mobilized. The superior aspect of the adrenal gland is then mobilized, taking care to divide the phrenic vessels supplying the gland. Once the superior and inferior borders of the gland are dissected adequately, attention is directed to the head of the gland, which is adjacent to the aorta. The left adrenal vein is divided if not previously done. The left adrenal artery arising from the aorta is next divided. The adrenal gland has

a highly variable vasculature, especially in larger lesions with increased blood supply. The use of a harmonic scalpel or hook cautery electrode can facilitate adrenal gland mobilization and adequately ligate small blood vessels supplying the gland.



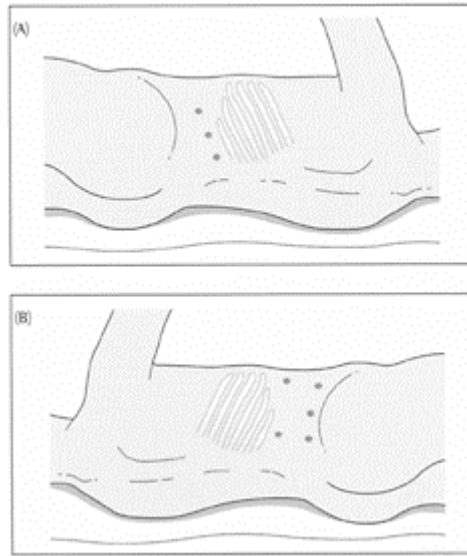
**Figure 49.8** Dissection of the left adrenal gland (1). The splenocolic and lienorenal ligaments are mobilized to allow the spleen (2) to be safely separated. If necessary, the tail of the pancreas (3) can be separated from Gerota's fascia. Medial dissection of the inferior border of the adrenal gland will eventually lead to the takeoff of the left adrenal vein (4) from the left renal vein (5).

Lastly, the lateral attachments of the adrenal gland are divided to fully free the gland from all surrounding tissues. The specimen is then placed into a retrieval bag and removed intact. Closure is similar to that for the right adrenalectomy.

#### *Retroperitoneal technique*

Patient positioning for the retroperitoneal approach differs from that for the transperitoneal approach. The patient is positioned in the full flank position with the table flexed. The primary port site is a 2 cm incision placed just below the tip of the 12th rib. A Hasson-type port is used here. Two additional ports are routine and a fourth port is optional. The port placement is similar on the right and left sides. Figure 49.9 shows the typical patient positioning and port placement for a laparoscopic retroperitoneal

adrenalectomy. The laparoscope is used through the primary port. The second port is placed posterior to the primary site, just below the angle formed by the 12th rib and the vertically-oriented paraspinous muscles. The third

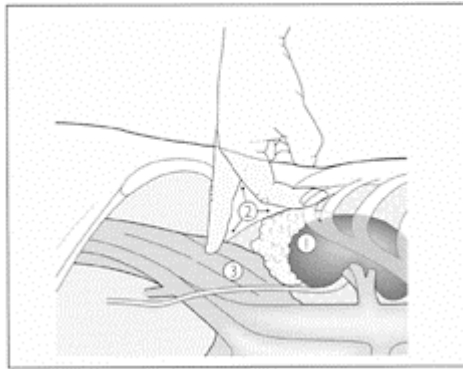


**Figure 49.9** The retroperitoneal approach for the left adrenal gland (A) and the right adrenal gland (B). The primary port site is placed just below the tip of the 12th rib for the laparoscope. A posterior port is placed just below the angle formed by the 12th rib and the vertically oriented paraspinous muscles. A third port is placed 3–4 cm medial and slightly superior to the primary site in the anterior axillary line.

port is placed 3–4 cm medial and slightly superior to the primary site in the anterior axillary line, taking care to avoid the peritoneal reflection. This arrangement allows the camera to sit between the two working ports to optimize orientation. The posterior port must not be too close to the psoas muscle, as the range of motion can be limited. These ports may be 3–10 mm, depending on the surgeon's preference and availability of instruments. We generally use two 5 mm ports, one 10 mm port, and one 12 mm port. This allows for accommodation of dissecting instruments, suction, and a clip applier. The optional fourth port may be used for retraction and is placed in the anterior axillary line,

about 5–7 cm inferior to the third port. An alternative is to use the two anterior axillary ports and omit the posterior port site.

Through the primary incision, a muscle-splitting dissection is performed with exposure created by S-retractors. Access into the retroperitoneal space is confirmed by inserting one finger and palpating the inner surface of the 12th rib above and the iliac crest below (Figure 49.10). This finger can also identify the psoas muscle and begin to sweep all anterior structures away. We prefer to create the retroperitoneal working space with a commercial dilating balloon (Origin Medsystems, Menlo Park, California). The trocar-mounted balloon is inflated posteriorly along the abdominal wall and cephalad from the incision, mobilizing Gerota's envelope with its contents away from the back wall. The Hasson port is then secured and the pneumoretroperitoneum is generated with carbon dioxide under 15 mmHg pressure. Additional ports are placed and secured as needed.



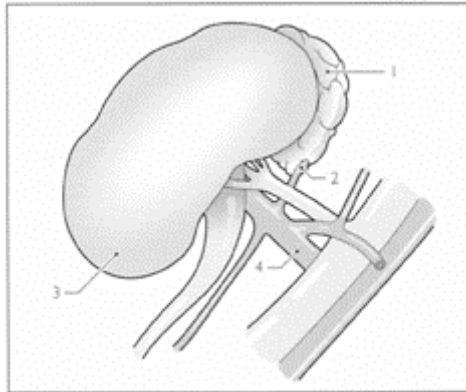
**Figure 49.10** Retroperitoneal access is obtained by making a 2 inch skin incision between the tip of the 12th rib and the iliac crest. All fascial layers are incised and the retroperitoneal space is digitally entered. The space is then further created by digitally identifying the psoas muscle (3) and the finger begins to sweep the peritoneum (2) medially away from the Gerota's fascia (1).

The key to the retroperitoneal approach is in understanding the orientation, which is distinctly different from the transperitoneal approach. Rather than looking down on the kidney and adrenal from above (very similar to an open transperitoneal view), we approach the kidney from behind with an end-on view of the lower pole. It is helpful if the balloon dissection is positioned up high to gain more rapid access to the adrenal

gland. Occasionally it is useful to reposition the balloon up higher and reinflate it. The initial view is nearly always somewhat tattered, but key landmarks can and must be identified. The psoas muscle is easily seen and serves as a guide for longitudinal orientation. Many random veils of tissue near the psoas can be swept aside or divided to clarify the view. Dissecting medially, the great vessels can be identified as they run parallel to the psoas fibers. The renal vessels are found by identifying the pulsations of the posteriorly situated renal artery, although exposure of these vessels is not always necessary. The kidney may be relatively difficult to identify if there is an abundance of perinephric fat. If the patient is thin and the adrenal mass prominent, locating the area of interest may be straightforward. However, a small adrenal mass in the midst of abundant fat can present a challenge. In these cases, intraoperative sonography is helpful.

### Left side

Once the initial dissection is complete and the appropriate landmarks identified, the adrenal gland must be located (Figure 49.11). Because there is often scant fatty tissue



**Figure 49.11** The retroperitoneal approach for the left adrenal gland (1). Initial dissection is cephalad along the psoas to the upper pole of the kidney (3). The adrenal vein (2) is often found along the inferomedial border. The adrenal vein can also be found by identifying the left renal vein (4) first.

posterior to the adrenal, the golden hue may be quickly noted. The dissection should be carried cephalad along the psoas to the upper pole of the kidney. We tend to approach the adrenal from a lateral angle and then find the adrenal vein along the inferomedial border, where it can be exposed, clipped, and divided. If locating the adrenal is difficult, or if the mass is a pheochromocytoma, the adrenal vein can be found first by identifying the left



renal vessels and locating the junction of the left adrenal vein with the left renal vein. Because the adrenal vein tends to course along the medial aspect of the kidney, the dissection must be kept strictly posterior. This keeps the kidney and adrenal from falling down into the field of view. After division of the adrenal vein, the remainder of the adrenal can be detached, remembering to lift and push, rather than grasp, the adrenal tissue. This reduces the risk of adrenal gland fracture and ensuing hemorrhage.

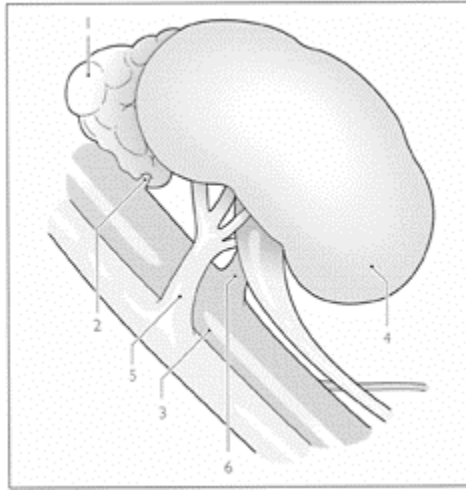
Once the adrenal is completely mobilized, the laparoscope is placed through one of the secondary ports so that the adrenal may be removed through the largest incision (the primary site). The adrenal is placed in a retrieval bag and removed. The port sites are closed in standard fashion.

### **Right side**

The right retroperitoneal adrenalectomy presents a challenge because of the position of the adrenal and the length of the adrenal vein in relation to the IVC (Figure 49.12). The same principles of retroperitoneal laparoscopy apply. Dissection moves cephalad along the psoas muscle, with careful attention to orientation. The kidney is held anteriorly by its own attachments or by an optional retractor. The adrenal gland must be located by dissection or by ultrasound before the adrenal vein can be approached. Identification and dissection of the IVC above the renal vessels may be helpful, but may also be treacherous. The right adrenal gland rests somewhat more medial to the kidney than the left adrenal gland, and the upper pole of the kidney may interfere with exposure of the adrenal gland. In addition, the right adrenal vein is situated on the far (medial) side of the gland, away from the dissecting instruments. Despite these challenges, once the adrenal is located, it can be mobilized and lifted anteriorly to expose the adrenal vein, which can then be clipped and divided. As with the other approaches, the remainder of the adrenal gland is mobilized with cautery and removed in a retrieval bag. The port sites are then closed.

### *Transthoracic technique*

Recently, the technique of thoracoscopic transdiaphragmatic adrenalectomy has been described.<sup>28</sup> This technique has potential for use when both the transperitoneal and



**Figure 49.12** The retroperitoneal approach for the right adrenal gland (1). The adrenal gland must be located by dissection or by ultrasound before the adrenal vein (2) can be approached. Identification of the venal cava is helpful (3). The right adrenal gland rests somewhat more medial to the kidney (4) than the left adrenal gland. The renal artery (5) and vein (6) are identified early in the dissection.

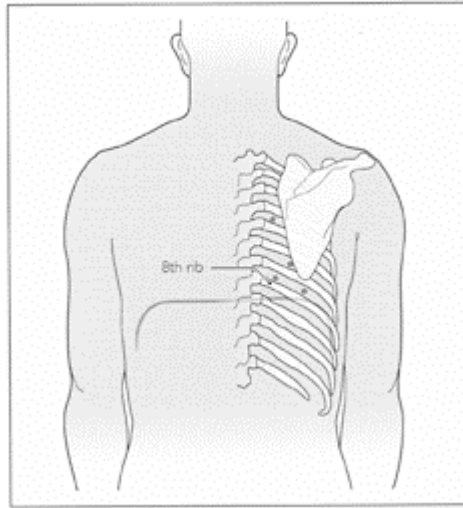
retroperitoneal spaces have been violated by prior surgery. Following double-lumen endotracheal intubation, the patient is placed in the prone position. A four port transthoracic technique is used (Figure 49.13).

In order to gain exposure to the adrenal gland, the diaphragm is incised under ultrasonographic guidance and the retroperitoneum entered. The adrenal gland is then identified and dissected free. Once the adrenal gland is removed, the diaphragm is repaired. A chest tube is kept in place at the conclusion of the procedure.

### Postoperative care

The advantages of the laparoscopic approach to the adrenal gland are immediately apparent in the postoperative period. The orogastric tube is removed immediately at the end of the case and the Foley catheter removed as soon as the patient is ambulatory. Postoperative pain is controlled with parenteral narcotics in the first 24 hours and

ketorolac or oral narcotics thereafter. Supplemental corticosteroids and appropriate antihypertensive medications are administered as needed, depending on the type of



**Figure 49.13** Trocar placements for thoracoscopic transdiaphragmatic adrenalectomy. This technique has potential for use when both the transperitoneal and retroperitoneal spaces have been violated by prior surgery. The patient is placed in the prone position. A four-port transthoracic technique is used.

tumor removed. Postoperative care can be coordinated in concert with an endocrinologist if necessary. Discharge is usually within 24–48 hours from surgery and full recovery requires 10–14 days.

### Complications

The most significant intraoperative complication is hemorrhage. The adrenal gland is highly vascular, which can result in troublesome bleeding if not adequately controlled.<sup>37</sup> The use of a harmonic scalpel during dissection of the adrenal gland can limit the amount of hemorrhage. In addition, the adrenal gland itself is very easily fractured, often resulting in bleeding.

Other intraoperative complications from laparoscopic adrenalectomy are similar to those for any laparoscopic procedure, and can include injuries to the colon, small bowel,

liver, gallbladder, spleen, and diaphragm.<sup>37</sup> In general, major complications occur less often as surgeon experience increases. Conversion to an open case should be done if hemorrhage is uncontrollable or intraoperative injury cannot be repaired through a laparoscopic approach.

**Table 49.3** *Selected laparoscopy adrenalectomy series*

| Author (year)                     | No. of cases | Age  | Approach                                | OR time (min) | EBL (ml) | Hospital stay (days) | Conversion rate | Complications  |
|-----------------------------------|--------------|------|---|---------------|----------|----------------------|-----------------|--|
| MacGillivray <sup>38</sup> (2002) | 60           | –    | Transperitoneal                         | 183           | 63       | 2                    | 0/60            |  |
| Valeri <sup>39</sup> (2002)       | 91           | –    | Transperitoneal                         | 92–148        | –3.5     |                      | 2/91            | 2 postoperative hemorrhage, 1 port-site bleed, 1 UTL, 1 death from myocardial infarction |
| Kebebew <sup>40</sup> (2002)      | 176          | –    | Transperitoneal                         | 168           | –1.7     |                      | 0/176           | 5.1%   |
| Lezoche <sup>35</sup> (2002)      | 216          | 45.9 | 149 transperitoneal, 67 retroperitoneal | 100           | –        | –                    | 4/216           | 1 death, hemoperitoneum, 1 wound infection   |
| Salomon <sup>34</sup> (2001)      | 115          | 49.3 | 115 retroperitoneal                     | 118           | 77       | 4                    | 1/118           | 3.5% intraoperative, 12.1% postoperative   |
| Guazzoni <sup>41</sup> (2001)     | 161          | 39.4 | Transperitoneal                         | 160           | –2.8     |                      | 4/161           | 5.5%   |
| Suzuki <sup>36</sup> (2001)       | 118          | 51.7 | 78 transperitoneal, 40 retroperitoneal  | 171           | 96.3     | –                    | 6/118           | 2 paralytic ileus, 4 shoulder tip pain   |
| Soulie <sup>42</sup> (2000)       | 52           | 46.9 | Retroperitoneal                         | 135           | 80       | 5                    | 1/52            | 5.7% intraoperative, 11.5% postoperative   |
| Mancini <sup>43</sup> (1999)      | 172          | –    | Transperitoneal                         | 132           | –5.8     |                      | 12/172          | 8.7%, 2 deaths   |
| Schichman <sup>44</sup> (1999)    | 50           | 54   | Transperitoneal                         | 219           | 142      | 3                    | 0/50            | 10%  |
| Winfield <sup>3</sup> (1998)      | 21           | 52.2 | Transperitoneal                         | 219           | 183      | 2.7                  | 0/21            | 1 subcutaneous bleed, 2 pneumothorax, 1 pulmonary edema                                  |
| Yoshimura <sup>4</sup> (1998)     | 28           | 42   | 11 transperitoneal,                     | 375           | 370      | 2.7                  | 0/28            | 4 blood transfusion, 4   |

|                                    |            | 17<br>retroperitoneal                 |       |        |                   | subcutaneous<br>emphysema, 2<br>postoperative<br>bleeding<br>1 pneumonia         |
|------------------------------------|------------|---------------------------------------|-------|--------|-------------------|--|
| Chee <sup>45</sup> (1998)          | 14 46.2 8  | transperitoneal,<br>6 retroperitoneal | 135   | Min 3  | 0/14              |  |
| Gagner <sup>46</sup><br>(1997)     | 100 46     | Transperitoneal                       | 123   | 70 3   | 3/100             | 12%; 3 DVT, 2<br>pulmonary<br>embolus  |
| Gasman <sup>33</sup><br>(1997)     | 23 49.6 23 | retroperitoneal                       | 97    | 70 3.3 | 0/23              | 1 postoperative<br>hematoma  |
| Terachi <sup>47</sup><br>(1997)    | 100 –      | Transperitoneal                       | 240   | 77 –   | 3/100             | –  |
| Rutherford <sup>48</sup><br>(1996) | 67 54      | Transperitoneal                       | 124   | – 5.1  | 0/67              | 3 DVT, 2<br>pulmonary emboli,<br>1 port-site hernia,<br>1 postoperative<br>bleed |
| Average                            | 47.1       |                                       | 153.5 | 98.6   | 36/1567<br>(2.3%) |  |

DVT, deep vein thrombosis; EBL, estimated blood loss; OR, operating room; UTI, urinary tract infection.

## Results

Worldwide experience with laparoscopic adrenal surgery has increased since its introduction in 1992. Several centers have now reported large series in the literature that document the decreased blood loss, shortened hospital stay, and faster return to normal activity. Selected recent series in the literature are summarized in Table 49.3.

Gagner et al reported on 100 consecutive laparoscopic adrenalectomy procedures performed through the transperitoneal approach.<sup>46</sup> The mean operative time was 123 min with an estimated blood loss of 70 ml. In their series, the open conversion rate was 3%, average length of hospital stay was 3 days or less, and morbidity was encountered in 12% of patients. The lesions removed included pheochromocytomas, aldosteronomas, Cushing's lesions, and others.

In the largest published series identified in the literature by Lezoche et al.<sup>35</sup> a total of 216 laparoscopic adrenalectomies were performed through the anterior transperitoneal, lateral transperitoneal, and the posterior retroperitoneal approaches. The study was a combined experience of surgeons in Italy and the Netherlands. The average operating time of all approaches was 100 min with a conversion rate of only 1.9%. Average hospital stay for all approaches was 3–4 days.

Comparison studies have been made between laparoscopic and open adrenalectomy to determine if there are significant benefits in the laparoscopic approach.<sup>2–9</sup> In general, the operative times for laparoscopic surgery are longer than for the open technique, particularly early on in the learning curve. However, the operative times decrease as surgeon experience increases. In addition, the laparoscopic approach offers less blood

loss, significantly less postoperative narcotic use, overall shorter hospital stay, and a faster return to normal activity. The cost of a laparoscopic adrenalectomy was shown to be comparable to that of an open adrenalectomy in one study.<sup>10</sup>

### **Laparoscopic adrenalectomy for malignant tumors**

Increased surgeon experience and comfort with laparoscopic adrenalectomies has led to performing laparoscopic adrenalectomies for larger and potentially malignant tumors. Henry et al<sup>50</sup> performed laparoscopic adrenalectomies on 19 patients with potentially malignant tumors, all of which were greater than 6 cm in size. Median operating time was 150 min, and conversion was necessary in 2 patients because of intraoperative evidence of invasive carcinoma. Six of the 19 patients had an adrenocortical carcinoma on pathologic diagnosis. One of these patients presented with a liver metastasis 6 months after surgery and died. The other 5 patients are alive, with a follow-up ranging from 8 to 83 months. The authors concluded that laparoscopic adrenalectomy can be performed on select patients in experienced hands; however, conversion to open adrenalectomy should be performed if there is evidence of local invasion observed during surgery.

Laparoscopic adrenalectomy has also been safely performed in patients with solitary adrenal metastases. In a recent series by Heniford et al,<sup>22</sup> laparoscopic adrenalectomy was performed in 11 patients, 10 of which had the adrenalectomy performed for metastatic disease. Average operative time was 181 min, and blood loss was minimal at 138 ml. One patient required conversion to an open approach due to local invasion of the tumor into the lateral wall of the vena cava, which was removed with the specimen. Ten of the 11 patients were alive, with a mean followup of 8.3 months. This data suggest that the laparoscopic approach to some malignant neoplasms, either originating from or metastasizing to the adrenal gland, is reasonable, but the conversion to an open procedure should be performed if local invasion is present.

### **Conclusion**

Laparoscopic adrenalectomy has become an accepted method for removing benign lesions of the adrenal gland. There is no question that the advantages of the laparoscopic approach include shorter hospitalization and convalescence. In addition, even hormonally active lesions such as pheochromocytomas can be safely approached laparoscopically. Relative contraindications to the laparoscopic approach include very large benign lesions and primary adrenal carcinomas. Both the transperitoneal and retroperitoneal techniques yield satisfactory results.

Laparoscopic adrenalectomy has been shown to be a safe and effective approach to many forms of adrenal pathology. It should be considered the standard of care in the management of benign lesions of the adrenal gland that require surgical removal.

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## Genitourinary trauma—minimally invasive alternatives

Michael Coburn

### **General concepts and history/evolution of management strategies**

The concept of minimally invasive surgery for trauma is a critical one. In many elective surgical settings, the advantages of a minimally invasive approach focus largely on the desire to minimize postoperative pain, accelerate postoperative return to full mobility and return to full function, minimize length of hospitalization, and minimize costs. In the setting of trauma management, the selection of minimally invasive therapy may mean the difference between minimal and excessive morbidity, or the difference between survival and mortality. The trauma patient is different from the elective surgical patient in many respects; most importantly, however, are two aspects of the trauma setting that make it critical to consider the most minimally invasive alternatives when selecting therapy. These are the realization that one is working with a compromised host, and the common presence of multiple, active, and potentially life-threatening injuries which must be addressed simultaneously and prioritized appropriately.

Many minimally invasive approaches to trauma management do not represent new areas of thinking. It has long been recognized that invasive approaches carry risks in the trauma patients and must be applied judiciously. Imaging for the accurate staging of injuries and selection of patients truly requiring operative intervention has developed along with the advent of the relevant imaging technology. Such technologies have allowed prudent, selective expansion of the indications for nonoperative management of injuries, such as splenic rupture or blunt renal injury, which were traditionally routinely managed operatively. Utilizing endoscopic, angiographic, or percutaneous techniques as minimally invasive alternatives to traditional open surgery has become routine in trauma management. The ready availability of interventional radiologic support in close physical and temporal proximity to the trauma center is a critical factor in applying minimally invasive management strategies.

The concept of damage control surgery for the management of the unstable trauma patient is an area of great interest among trauma surgeons. This strategy involves the concept that limiting initial operative objectives to the control of life-threatening hemorrhage and continued fecal and urinary spillage, followed by resuscitation, with delayed surgical management of non-life-threatening injuries to a subsequent operative setting, will reduce morbidity and mortality. The goal in this form of management is to avoid the 'lethal triad' of progressive coagulopathy, hypothermia, and acidosis which may result in early mortality if too aggressive an effort to complete all reconstructive operative tasks is made in the setting of continued blood loss in the immediate post-injury

period. This approach has gained wide acceptance among general trauma surgeons and is being applied among surgical specialty services as well.<sup>1</sup>

Iatrogenic trauma represents an area in which minimally invasive interventions may be applicable. Stenting and diversion may allow avoidance of surgical exploration and repair in selected cases and early experience with laparoscopic approaches to iatrogenic ureteral and bladder trauma is evolving.

### **Diagnosis and imaging**

Accurate imaging and staging of urologic injuries is an important component of trauma management. Developments in imaging technology have impacted greatly on the urologist's ability to minimize unnecessary explorations for injuries, which, based on imaging criteria, will likely resolve with nonoperative management or be amenable to management with minimally invasive techniques.

#### *Upper tract imaging*

The contrast-enhanced computed tomography (CT) scan has become the standard means of renal imaging in cases in which indications exist for imaging after blunt trauma. The presence of gross hematuria, or the presence of microscopic hematuria with hypotension at any time following injury, should prompt such imaging.<sup>2</sup> Some authors have suggested expanding these imaging criteria to include microscopic hematuria alone if there is a history of deceleration injury, long bone, spinous process or lower rib fracture, or head or other neurologic injury such that accurate physical examination data are unobtainable. Using these imaging criteria following blunt renal trauma reduces the unnecessary morbidity of performing contrast imaging for all blunt trauma patients, selecting those with an increased risk of significant renal injury. Several studies have demonstrated the safety of limiting imaging selection criteria in this manner. There remains controversy in the pediatric setting; some authors recommend a more liberal approach for imaging in the pediatric patient with microscopic hematuria alone, because of the increased risk of ureteropelvic avulsion, pelvic rupture, or forniceal avulsion injuries which may present in the absence of more significant hematuria. Others suggest that differing criteria—e.g. 50 red blood cells (RBCs) per high power microscopic field—may be an appropriate criterion to justify imaging, while still others suggest that the adult criteria may be safely applied.<sup>3</sup>

The CT scan has a number of advantages over other imaging options. The size of a perinephric hematoma is clearly demonstrated, and renal perfusion or contrast extravasation is easily detected. The presence of nonurologic injuries is also more reliably seen than with other approaches. In the absence of the availability of CT, or when the patient is taken immediately to the operating suite prior to obtaining imaging studies, the 'one-shot IVP' (intravenous pyelography) is applicable. This can be obtained in the shock room or on the operating table, following the infusion of intravenous contrast (2 ml/kg) with a 10 min film being obtained. The presence of two functioning renal units, the presence or absence of gross extravasation, or the presence of a grossly

abnormal collecting system on the side of a suspected injury may help plan surgical intervention.

One potential pitfall of modern CT scanning for trauma is the rapidity of the spiral scanners. The scanning series in modern units may be completed prior to contrast excretion throughout the collecting system and ureter. It is important to request that an excretory phase be obtained, as extravasation from the intrarenal collecting system or from the ureter can be missed unless a late phase, which demonstrates opacification of the ureter down to the bladder, is consistently obtained in the trauma setting. Avulsion or transection of the ureter may not be appreciable without contrast excretion, urinoma may be mistaken for hematoma, and critical injuries missed without proper protocols for trauma CT scanning.

For penetrating trauma, any degree of hematuria should prompt imaging, if feasible, prior to surgical exploration. Staging renal injuries prior to laparotomy may allow selection of definitive nonoperative management of upper tract injuries and avoid unnecessary renal exploration. When no laparotomy is planned and the urologist must determine if any indication for abdominal surgery exists based on the status of the upper urinary tract (tangential flank gunshot wound, posterior stab wound), staging the injury with CT scanning is critical to patient selection. If no imaging is obtainable before laparotomy, as mentioned above, the intraoperative IVP may be helpful in demonstrating the presence of a normal kidney contralateral to the side of injury, prior to renal exploration.

Appropriate upper tract imaging plays a central role in the minimally invasive approach to managing urologic trauma, as such imaging guides the selection of nonoperative management or the institution of minimally invasive therapeutic approaches vs operative exploration. While some authors maintain that only hemodynamic instability will mandate operative exploration for renal trauma, the demonstration of a grade V renal parenchymal injury, renovascular injury, or extensive collecting system or ureteral injury is important in planning optimal patient management; imaging data are critical for defining such injuries.

### *Lower tract and genital imaging*

When bladder injury following blunt trauma is suspected by the inability to void, the presence of gross hematuria, or the presence of pelvic fracture, the stress cystogram is the standard approach for imaging. As most extraperitoneal bladder injuries are manageable with catheter drainage alone, while nearly all intraperitoneal ruptures are managed with operative repair, radiologic staging of bladder trauma is essential in selecting minimally invasive management. A stress cystogram may be performed using static radiologic, fluoroscopic, or CT techniques. The most common approach has been the static radiologic cystogram, although currently, with CT scanning being so frequently employed in the evaluation of blunt trauma patients, CT cystography is being more commonly utilized; the urologist should be thoroughly versed in the interpretation of any of these studies. An adequate stress cystogram technique must be utilized, regardless of which of the above imaging modalities are employed. This requires inserting a Foley catheter, followed by filling the bladder to one of several endpoints: a standard volume (300–400 ml in the adult), maximal filling by gravity, or a point of perceived fullness by

the patient. In the static cystogram approach, vertically oriented radiographs are obtained before infusion, with a full bladder, and after contrast drainage and washout. The CT obviates the need for the washout film, as the space anterior and posterior to the bladder is shown on the filling phase scans. Patterns of extraperitoneal vs intraperitoneal extravasation are well described. In addition, bladder contusion, displacement, bladder neck injury, or avulsion may also be suspected from cystographic findings.

In penetrating injuries to the pelvis, it is often appropriate to forego bladder imaging if surgical exploration at the time of laparotomy is planned, regardless of the imaging findings.

If there is clinical suspicion of urethral injury, or blood is present at the urethral meatus, a retrograde urethrogram should be obtained before any attempt at Foley catheter insertion, to avoid further complicating a urethral injury. Complete or incomplete disruption injuries of the anterior or posterior urethra may be demonstrated on retrograde urethrography; such information is essential to selection of management.

Blunt trauma to the genitalia is another area in which imaging may be very useful in selecting operative vs nonoperative management. Blunt scrotal trauma is accurately imaged by scrotal ultrasonography. Ultrasound may demonstrate evidence of testicular rupture (loss of homogeneity of testicular parenchyma, loss of continuity of tunica albuginea), prompting operative repair. Hematocele (blood within the tunica vaginalis cavity) or intratesticular hematoma may also be noted on ultrasound examination. Penetrating injuries to the genitalia are generally explored surgically, so imaging is of little value in this setting.

### **Operative versus nonoperative management**

As alluded to in the imaging section above, selection of operative vs nonoperative management strategies for urologic injuries is a central issue in the discussion of minimally invasive approaches to trauma. Much of the data upon which currently accepted approaches have developed is retrospective and consists of small case series or case reports. Efforts to achieve a consensus in this controversial area through extensive literature review and meta-analysis are ongoing.<sup>4</sup>

The importance of selecting operative vs nonoperative approaches in urologic trauma varies with the clinical setting and the site of planned exploration. A negative scrotal exploration carries very little morbidity for the patient. A negative abdominal exploration, however, exposes the patient to significant risks. Organ salvage is also a critical factor. It has been demonstrated that a nonoperative approach to testicular rupture or blunt penile fracture carries significantly higher complication rates than early repair; the likelihood of orchiectomy is far greater with nonoperative management as well.<sup>5</sup> With renal exploration, however, the reconstructive challenges are far greater and may involve significant blood loss. While some experienced urologic trauma surgeons have reported very low nephrectomy rates, in the range of 10%, following renal trauma exploration, many other centers report much higher rates of renal loss. While it is difficult to strictly compare ultimate renal loss rates with an aggressive operative approach vs a highly selective nonoperative approach, the literature suggests that, in many centers, renal exploration carries a higher nephrectomy risk than nonoperative management for all but

the highest grades of injury. It is therefore critically important to be as selective as possible in choosing which kidneys to explore vs which to observe. Whether a particular renal injury is amenable to observation alone, minimally invasive therapeutic management (embolization, drainage procedures) or requires operative repair or removal is a multifactorial judgment which is addressed below, by specific organ site.

### **Minimally invasive options, by organ site**

#### *Kidney*

As mentioned above, staging renal injuries with imaging modalities is an important element in selecting operative vs nonoperative management. Renal injuries may be selected for operative management for several reasons, based on clinical or hemodynamic factors or on specific anatomic factors of the injury. The considerations are different if complete radiologic staging is, or is not, obtained prior to laparotomy.

It is generally agreed that upon laparotomy, if a pulsatile or expanding perinephric hematoma is encountered or there is active bleeding into the abdominal cavity from the renal fossa, exploration with surgical repair or removal is indicated. Temporizing measures in this setting are addressed below under 'damage control' considerations. If, alternatively, the kidneys are not staged preoperatively with imaging studies, and a perinephric hematoma is nonexpanding, nonpulsatile, and there is no free bleeding into the abdominal cavity, whether to explore the kidney remains controversial. While some authors suggest that in this setting all kidneys should be explored, most reports suggest that for blunt trauma a selective approach is appropriate. The intraoperative IVP may be helpful in this setting. If it shows the kidney on the side of the injury to have a normal parenchymal outline with a normal appearing collecting system, the likelihood of encountering an injury requiring operative repair is thought to be low and foregoing exploration may be preferable. Marked distortion of the collecting system, contrast extravasation, or nonvisualization predict a high likelihood of there being an injury which will profit from exploration and repair, and proceeding with operative exploration may be of benefit, assuming the patient is stable to undergo such exploration and needed repair. If nonexploration is selected, postoperative CT scanning is helpful to define the features of the injury and plan definitive management. For penetrating renal trauma, similar considerations apply, although some authors maintain that a lower threshold for exploration of the injured kidney in the penetrating trauma setting is desirable. This perspective maintains that the risk of renovascular injury or extrarenal collecting injury is higher when the kidney is damaged by a penetrating object or missile than when blunt forces are responsible. Damage control options for penetrating renal injuries are discussed below.

If renal injuries are managed without initial surgical exploration, minimally invasive interventions may, in selected cases, be applied proactively. For high-grade injuries due to renal stab wounds, for example, a high risk of bleeding may be anticipated because of the size of the hematoma or trajectory of the injury (deep parenchyma, proximity to renal sinus structures). In such cases, early arteriography with embolization of violated arterial branches may be preferable to proceeding with such intervention emergently when a

delayed bleed occurs. When nonoperative management is selected, patients with significant renal trauma should be carefully observed for post-injury complications that may require intervention.

### *Ureter*

Blunt injuries to the ureter are rare; those that involve ureteral or ureteropelvic avulsion from blunt forces are best repaired early using standard surgical techniques. Most such patients will have associated injuries and laparotomy may be indicated for other reasons as well. Literature on the topic suggests that early operative repair of blunt ureteral injuries produces superior results to stenting or nephrostomy diversion with delayed repair. The latter approaches are more applicable to the setting of missed injuries and delayed recognition, where diversion and late reconstruction are preferable, depending on the time considerations and clinical status of the patient (see below).

Penetrating injuries to the ureter are also best managed by early operative exploration and repair. Simply stenting ureteral gunshot wounds carries a high stricture and late nephrectomy rate; excision and primary repair or ureteral reimplantation into the bladder are the standard approaches in these situations. As for blunt trauma, missed injuries with delayed recognition are the settings in which such minimally invasive approaches are applicable.

When stenting or percutaneous diversion is selected as initial management for ureteral injuries, several technical points must be kept in mind. Retrograde pyelography may be useful in the setting of a suspected missed ureteral injury to clarify the findings on CT scan or IVP. If the patient is in a stable clinical state to tolerate a trip to the operating room, retrograde pyelography and an attempt at retrograde stent insertion offers the advantage of providing definitive diagnostic information regarding the level of and completeness of the injury. When extravasation is present but continuity of the ureter is preserved, retrograde stenting can be achieved in most cases. Extravasation may cease more rapidly if a Foley catheter is left indwelling as well, to prevent reflux and exposure of the ureteral injury to bladder pressures during voiding. If a urinoma is present, percutaneous drainage may be performed under CT or ultrasound guidance. If, for whatever reason, cystoscopy and retrograde stenting attempts are felt to be ill-advised, either due to the patient's instability or lack of ready access to the operating room, percutaneous drainage via nephrostomy tube insertion may be selected. In this case, an attempt may be made initially to pass a guide wire across the injury into the bladder, followed by insertion of a universal stent or 'nephrostent', which allows for either internal drainage when capped externally, or external drainage when attached to a collection device. If there are signs of sepsis, or if minimization of initial manipulation is preferred, a simple nephrostomy tube may be inserted initially, with a secondary attempt at universal stent placement reserved for a later setting when the patient is in more suitable condition for such an attempt.

### *Bladder*

Bladder injuries may be divided into several categories which are relevant for a discussion of selecting minimally invasive management. Intraperitoneal and

extraperitoneal ruptures, combined injuries, bladder neck avulsion injuries, bladder contusions, and penetrating injuries should all be addressed in this context.

Intraperitoneal bladder rupture, which generally occurs due to blunt trauma with sudden compression of the full bladder and laceration of the bladder dome, is nearly always managed with operative repair. Patients present with inability to void or with gross hematuria. Diagnosis is usually made on cystography, on abdominal CT, or by a grossly positive peritoneal lavage. As urine enters the abdomen following this injury, evacuation of urine and clots from the peritoneal cavity with operative repair of the laceration is necessary. There is interest in using laparoscopic techniques to accomplish this task, and simple endosuturing can certainly be applied to close the bladder dome injury. At this time there is little experience in this area, except in the setting of minimal iatrogenic injuries where there have been several reports of successful laparoscopic repair. In the setting of acute trauma, most trauma surgeons prefer laparotomy with inspection of the abdominal viscera to rule out concomitant hollow viscus rupture, with open bladder repair. This can be accomplished via a lower abdominal midline incision.

Extraperitoneal bladder rupture, on the other hand, is most often managed with minimally invasive techniques. This injury usually occurs in the setting of a pelvic fracture, and again is diagnosed by cystography, prompted by the presence of gross hematuria, which is present in over 95% of cases. Corriere and others<sup>6</sup> have demonstrated that the significant majority of extraperitoneal bladder rupture injuries can be managed with the minimally invasive approach of utilizing Foley catheter drainage alone. A large-bore catheter (generally 20–24F) is inserted. Eighty to ninety percent of such injuries are healed within 10–14 days; stress cystography is obtained prior to catheter removal. If extravasation is no longer evident, the catheter is removed. In 10–20% of cases, additional time is needed to allow full healing, and the catheter is then left in place for another week with repeat of the cystogram. While this approach is applicable in most cases, there are specific indications for operative repair for extraperitoneal rupture. These include persistent troublesome hematuria resulting in catheter occlusion; the presence of a concomitant vaginal or rectal injury; open pelvic fractures in continuity with the bladder injury; and surgical exposure of the injury for another indication. If surgical repair of the bladder following extraperitoneal rupture is necessary, it is generally repaired through a high cystotomy incision with transvesical suturing of the injury, rather than through a retropubic approach, which can require entering the retropubic hematoma, risking significant and potentially uncontrollable bleeding.

Bladder neck avulsion injuries, more common in the pediatric setting and also usually associated with pelvic fracture, should be repaired surgically when the patient is hemodynamically stable to undergo such repair.<sup>7</sup> A cystostomy may be performed initially as a temporizing measure, and has the advantage of minimizing the risk of extensive bleeding from the pelvic hematoma associated with immediate post-injury repair attempts. Outcomes for early (24–72 hours post-injury) repair of these injuries appear superior to late repairs following suprapubic diversion and allowing an obliterated stricture to form, in terms of voiding function and continence.

Bladder contusions, diagnosed by the presence of hematuria of bladder origin but with a negative cystogram, are routinely managed with catheter drainage as well.

Although penetrating bladder injuries are usually repaired surgically in the setting of laparotomy for associated injuries, selected cases may be manageable nonoperatively



with catheter drainage alone if it can be reliably demonstrated that the bladder defects are small, and there is no intraperitoneal, rectal or vascular injury present. Both invasive and noninvasive imaging may be necessary to appropriately select such patients for nonoperative management, possibly including abdominal CT scanning, peritoneal lavage, arteriography, proctoscopy, and cystoscopy with retrograde pyelography.<sup>8</sup>

### *Urethra I and external genitalia*

Minimally invasive approaches to the initial management of urethral and genital injuries are very relevant for several reasons. Injudicious manipulation of the injured urethra may produce further injury and may complicate an already complex problem. The importance of preserving injured genital tissues with observation for questionable viability is also an important principle of management which improves functional and cosmetic outcome. Urethral and genital injuries presenting in a community setting are often best managed with conservative, temporizing measures until specialty expertise is available.

Suspected urethral rupture injuries are diagnosed on retrograde urethrogram. Complete ruptures are recognized by extravasation of contrast, with no contrast passing beyond the injury to the proximal urethra or bladder. Incomplete injuries demonstrate extravasation, with contrast also entering the proximal urethra or bladder. For incomplete injuries to the posterior or anterior urethra, urethral catheter insertion is reasonable, and is most safely performed by cystoscopic guidance with passage of a guide wire across the injury. A council-tip catheter or standard Foley catheter with a hole punched in the tip may then be passed over the guide wire.

Posterior urethral disruption injuries which are complete are traditionally managed with suprapubic cystostomy placement and delayed urethroplasty following 3–6 months of diversion. Most such injuries occur following pelvic fracture, especially those with large pubic diastases or vertical shear injuries. Many such patients may be hemodynamically unstable and their injuries must be prioritized. Over the past decade there has been increasing interest in early catheter realignment for such injuries, in an effort to shorten the period of catheterization and reduce the need for delayed urethroplasty.<sup>9</sup> A variety of methods for achieving catheter realignment have been utilized. Patients must be carefully selected for such interventions; catheter alignment attempts should generally be delayed (24–72 hours) until the patient is hemodynamically stable. The most commonly described approach involves achieving percutaneous access to the bladder and, with simultaneous antegrade and retrograde cystoscopic guidance, passing a guide wire across the injury and placing a catheter transurethrally over the wire. Overall, approximately 50% of patients managed in this manner may ultimately achieve stabilization of their stricture without requiring urethroplasty, but multiple procedures such as direct-vision internal urethrotomy (DVIU) and dilation are often needed to reach this point.

Complete anterior urethral ruptures, typically seen following straddle-type injuries, are best managed with suprapubic diversion and delayed urethroplasty. It is difficult in the acute trauma setting to know how much urethra must be debrided, as there is often extensive crush injury and perineal hematoma. Delaying definitive repair in this setting generally produces better outcomes than initial surgical intervention. An exception is in the penetrating trauma patient; in this case, initial operative repair and limited

debridement or suturing of the defect is associated with favorable outcomes and may be selected if the patient is appropriately stable for such intervention. For anterior urethral injuries in which there is significant urethral loss, bringing both ends to the overlying skin with a plan for delayed reconstruction is preferable to early, complex reconstructive efforts in the contaminated field of a penetrating injury.

Genital injuries are most often managed with early operative repair. Blunt penile fracture and testicular rupture injuries have far better outcomes in terms of both function and organ salvage with early operative repair as compared with nonoperative management.<sup>10</sup> Nearly all penetrating injuries to the penis or scrotal contents should be managed with operative exploration and repair. Conservative approaches are appropriate to major soft tissue injuries of the genitalia where the viability of injured tissues is uncertain. Placement of moistened dressings with interval reassessment may be the best means of initially managing such injuries; one should be very conservative in debriding injured genital tissue until vascular status has declared itself in the early days following injury.

### **Minimally invasive options for management of complications of trauma**

Dealing with complications of urologic trauma is an important application for minimally invasive techniques. Some of the settings in which complications may be appropriately managed with minimally invasive approaches include renal or pelvic bleeding, post-repair extravasation, catheter dislodgement, and urinoma and abscess formation. Many of these approaches are equally applicable in the nonurologic trauma setting.

In cases of persistent or delayed bleeding from an injured kidney, angiographic embolization is an important management alternative. Whether to proceed emergently to surgery or attempt embolization depends on several factors, including the relative availability of surgical or radiologic facilities and expertise, as well as the task to be accomplished. If bleeding is the only problem requiring intervention, embolization is a very desirable approach. If, on the other hand, debridement of necrotic tissue or control of continued urinary extravasation is necessary, a surgical approach may more expeditiously accomplish the objectives. Subselective embolization is preferable if the kidney is otherwise salvageable. If the kidney is severely injured—grade IV or V injury by AAST (Association for the Surgery of Trauma) criteria—and nephrectomy is contemplated, embolization of the main renal artery with planned subsequent nephrectomy may still be appropriate, depending on the resource availability issues noted above.

Angiography with embolization is also an important option in pelvic bleeding following pelvic fracture. Specific embolization of actively bleeding internal iliac artery branches is generally feasible in the trauma setting. Placement of an external pelvic fixator device may also contribute to the control of troublesome pelvic bleeding following pelvic fracture.

Urinary extravasation following repair of renal or ureteral injuries is not uncommon, and does not always require intervention. If extravasation is minimal and asymptomatic, observation may be appropriate. If extravasation is high-volume and persistent, if there

are infectious concerns, or if a urinoma develops, drainage is desirable. Retrograde stent placement generally with a concomitant Foley catheter placement is appropriate; it is critical, however, to verify that the stent is fully within the collecting system and does not exit from the repair site into the retroperitoneum. Depending on the individual anatomy and location of the leak, antegrade nephrostomy placement may be preferable, though it can be difficult in the absence of any collecting system dilatation. This situation does not arise frequently following ureteral repairs, since stent placement is a routine part of such repairs. If the stent becomes occluded or migrates or otherwise fails to drain and extravasation persists, antegrade nephrostomy placement is usually the best recourse.

Complications of bladder, urethral, and genital injuries are generally managed conservatively or may require reoperation, as in the case of persistent bleeding, wound dehiscence, etc.

### **Damage control surgery—relevance to urologic decision making**

Damage control surgery for trauma is an important innovation in trauma management; the urologic trauma surgeon must be familiar with the rationale, principles, and practice of damage control approaches in order to cooperate effectively with the general trauma surgeon in the overall management of the unstable trauma patient.

Damage control surgery represents an approach to management of the critically injured patient in which there are specific, limited goals which are to be accomplished during the initial operative intervention, with other tasks being accomplished at a subsequent setting. The principles were originally applied to penetrating abdominal trauma and have been generalized to include other forms of complex injury. In the unstable trauma patient, the focus is on control of life-threatening hemorrhage and prevention of continued fecal contamination through an abbreviated laparotomy; non-life-threatening injuries are handled at a separate operative setting. The patient is taken to the intensive care unit following the initial laparotomy for resuscitation; when specific endpoints are reached, delayed operative maneuvers may be accomplished upon return to the operating room.

The physiologic rationale for damage control surgery is to avoid the so-called lethal triad which develops when prolonged initial operative procedures are performed in the unstable trauma patient. With continued blood loss and repeated transfusion, patients develop progressive hypothermia, acidosis, and coagulopathy, which can result in the patient's demise. Damage control surgery seeks to avoid the lethal triad by focusing on the limited goals of stopping serious surgical bleeding and controlling continued fecal contamination at the initial operative setting. The operative management of injuries not immediately life-threatening is delayed until the patient has undergone appropriate resuscitation and is in an appropriate physiologic state to tolerate the additional time required to perform the needed additional surgical tasks which were delayed at the initial operative setting. Commonly utilized initial operative maneuvers may include packing of solid viscera, temporary ligation of injured bowel segments, and the use of vascular shunts. Often, temporary abdominal closure techniques are implemented (skin-only closure, Bogota bag, or plastic silo closure) when secondary laparotomy is anticipated.

The urologist must also employ strategies to prioritize injuries and potentially delay diagnostic and therapeutic interventions in the damage control setting. Among the options available to the urologist are choosing not to explore a perirenal hematoma at initial laparotomy if it is not rapidly expanding, and instituting temporary urinary diversion for ureteral or bladder injury when the patient is too unstable to undergo primary repair (Figure 50.8). Urologic experience with damage control strategies has been published and appears to result in reduced mortalities in trauma patients compared to traditional approaches, as has been demonstrated in the general trauma surgery literature as well.<sup>11</sup>

### **Laparoscopic applications for urologic injuries**

While in some contexts, the concept of minimally invasive surgery is synonymous with laparoscopic surgery, our discussion of minimally invasive approaches to urologic trauma has been more inclusive. Although there has been relatively little work done on the laparoscopic applications for urologic trauma, there is a growing literature on this topic, and there are several settings for which laparoscopic techniques have not been extensively utilized but may potentially be highly applicable.

In the broader area of abdominal trauma, minimally invasive diagnostic approaches are central to current diagnostic approaches. The use of peritoneal lavage to determine the need for laparotomy is well-established. The FAST (Focused Abdominal Sonography for Trauma) examination, utilization of abdominal ultrasound by the surgeon in the emergency center, to detect the presence of free fluid in the abdominal cavity, for example, has also become very popular and there is a growing literature supporting its usefulness. The use of diagnostic laparoscopy, either in the traditional operating room environment or in the shock room using small-caliber ports and instrumentation, is an area of active clinical research in a number of trauma centers, and may ultimately play an important role in injury detection and staging.<sup>12,13</sup>

Depending on the specific anatomic area of interest, laparoscopy may readily determine if the peritoneal cavity is violated, allowing planning for definitive exploration. Challenges have been met in effectively 'running the bowel', or assessing the entire intestine for injury, but improving laparoscopic retractor systems and instrumentation are enhancing the feasibility of such techniques. The question of when it is truly to the patient's advantage to undergo laparoscopy in the abdominal trauma setting is complex, however. One must consider the logistical demands of performing laparoscopy at odd hours and in a busy trauma center, the potential delay which it may cause in offering definitive therapy, and the cost and the true potential reduction in morbidity when addressing the role of laparoscopy in abdominal trauma.

For urologic injuries, laparoscopy is certainly applicable to the repair of certain bladder injuries and ureteral injuries, if adequate dissection and endosuturing techniques are available. Particularly in the setting of suspected or diagnosed iatrogenic trauma, the minimally invasive approach may be appealing. There is apparently an increasing incidence of iatrogenic urinary tract injury being observed nationally with the growing number and complexity of laparoscopic gynecologic and general surgical procedures being performed. Laparoscopic repair approaches to bladder and ureteral trauma are particularly relevant in this setting. Just as laparoscopic pyeloplasty and

ureteroureterostomy in the elective setting are being more commonly performed, ureteral mobilization and repair in the trauma setting are potentially equally feasible. Ultimately, progress in the quality of instrumentation and greater familiarity with potential applications, translated from the elective to the emergency surgical setting, will help determine the appropriate role of laparoscopic surgery for urologic trauma.

### Conclusions

Minimally invasive management of urologic trauma represents an evolving area of clinical care, with new diagnostic and treatment approaches being evaluated as technology progresses. The utilization of interventional radiologic, endoscopic, and laparoscopic approaches to managing traumatic injuries offers great promise in reducing morbidity for trauma patients. Clinical judgment is critical in assessing the apparent benefit of minimally invasive manipulations vs traditional surgical approaches. A cooperative approach to working with the general trauma surgeon on the patient with multiple injuries is also of central importance in selecting patients for minimally invasive management strategies.

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## Minimally invasive uses of intestinal segments for urinary diversion

Sidney C Abreu and Inderbir S Gill

### **History of urinary diversion:**

Bowel segments have been used throughout the years for various reconstructive urologic applications. The stomach, jejunum, ileum, and colon have been successfully employed for bladder augmentation and bladder replacement. The initial clinical attempts to drain urine into the rectosigmoid were performed in the 19th century.<sup>1</sup> As the indications for cystectomy increased, so did the necessity to develop an optimal technique of urinary diversion. Remarkable surgical innovation has recently made possible the development and widespread use of orthotopic neobladder techniques.<sup>1</sup> Approaching the beginning of this new millennium, urologists have begun to explore minimally invasive techniques to urinary diversion.<sup>2,3</sup> Laparoscopy has been applied in an attempt to reduce the morbidity resulting from bladder removal and substitution. To date, various techniques of urinary diversion have been performed laparoscopically, either completely intracorporeally or by laparoscopic-assisted techniques.<sup>4,5</sup>

In this chapter, we describe the morphologic and physiologic aspects related to urinary diversion in general. Following this, the worldwide available clinical experience with laparoscopic use of various bowel segments is reviewed. Finally, experimental minimally invasive approaches related to urinary diversion are also presented briefly.

### **Applied anatomy of the stomach, and small and large bowel, as used for urinary diversion**

#### *Stomach*

The stomach is a well-vascularized organ that receives most of its blood supply from the celiac axis. Maintaining the gastroepiploic vessels that supply the greater curvature of the stomach as a pedicle, a vascularized stomach patch consisting of the entire antrum pylori or a wedge of the fundus can be mobilized to the pelvis. Furthermore, the stomach has a thick seromuscular layer that can be separated from the mucosa, thus facilitating a submucosa ureteral reimplantation when required.

#### *Colon*

The colon requires mobilization from its fixed position to achieve the mobility necessary for the reconstructive procedures. The larger diameter of the colon when compared to the ileum may be an advantage. Preservation of an intact ileocecal valve may help to avoid diarrhea and excessive bacterial colonization of the ileum.

*Ileum*

The ileum is a preferred segment of bowel that has been employed in various types of urologic reconstructive procedures. It is mobile, has a constant blood supply, its shape is ideal for conduit formation, and it has enough redundancy to allow various lengths of segments to be used without compromising the host. Occasionally, the mesentery may be short, which makes its mobilization into the deep pelvis difficult.

**Physiologic considerations**

Selection of the appropriate intestinal segment must consider the physiologic properties unique to the stomach, jejunum, ileum, and colon. In each case, the ideal bowel segment must fit the patient's condition, the renal function status, and type of diversion required.

*Metabolic implications***Ileum and colon**

Reabsorption of urinary ammonia and ammonium chloride by the ileal and colonic segments produces hyperchloremic metabolic acidosis. Although such acidosis occurs in most patients, it is generally of minor degree.<sup>6,7</sup> Severity of hyperchloremic metabolic acidosis depends on the period of contact between the urine and the intestinal mucosa, as well as the length of bowel segment used. Severe metabolic acidosis is manifested by patient weakness, fatigue, polydipsia, and anorexia. Chronic metabolic acidosis causes mobilization of calcium carbonate from bone. The carbonate combines with hydrogen while the calcium is excreted in urine, whereas can result in osteomalacia.<sup>8</sup>

**Stomach**

When the stomach is employed, the gastric mucosa acts as a barrier to chloride and acid reabsorption. However, due to the secretory nature of the gastric mucosa, hypochloremic hypokalemic metabolic alkalosis may occur. Also, in cases of gastrocystoplasty, hematuria-dysuria syndrome may occur.<sup>9</sup> However, in most patients these symptoms are intermittent and mild, and do not require treatment.

**Jejunum**

The jejunum is usually not employed for reconstruction of the urinary system because it potentially can cause severe electrolyte disorders such as hyponatremia, hypochloremia, hyperkalemia, azotemia, and acidosis. Rarely, when the jejunum is the only segment available, a portion of the jejunum as distal as possible should be used to minimize problems with electrolyte imbalance.<sup>10</sup>

*Mechanics of tubular and detubularized bowel***Volume-pressure considerations**

Configuration of the selected segment of bowel directly impacts upon the reservoir volume-pressure characteristics. Laplace's law states (for a sphere) that the tension of its wall is proportional to the product of the radius and pressure. Thus, theoretically, for a given wall tension, the greater the radius, the smaller the generated pressure. Therefore, detubularization of the bowel segment along its antimesenteric border and creation of a spherical reservoir should be the goal, aiming to preserve the upper urinary tract and to prevent incontinence.

**Motor activity**

The impact of detubularization upon motor activity of the bowel is unclear. Theoretically speaking, splitting the bowel along its antimesenteric border should discoordinate its motor activity, thus decreasing the intraluminal pressure. Experimental and clinical data suggest that the motor activity is markedly interrupted following the detubularization, resulting in fewer or ineffective contractions of the reservoir walls. However, over a period of 3 months, peristaltic waves reappear, returning to their normal coordinated status.<sup>12</sup>

*Renal functional considerations*

Although urinary diversion in and of itself may compromise renal function, a certain robust baseline renal reserve is necessary to efficiently eliminate the excess of urinary solutes reabsorbed by the employed intestinal segment in order to prevent potentially serious metabolic sideeffects.<sup>12</sup> The level of renal function required to safely perform a urinary diversion depends on the amount of bowel used for the diversion as well as the length of time that the urine stays in contact with intestinal mucosa. Thus, a higher baseline renal reserve is necessary for continent reservoirs than for short conduits. However, as a general rule, patients with serum creatinine below 2.0 mg/dl tolerate intestinal interposition in the urinary tract well.<sup>12</sup>

**Patient selection for laparoscopic urinary diversion**

Proper patient selection is crucial to achieve good surgical outcomes. The criteria for selection of the type of urinary diversion have been outlined above. Furthermore, the criteria for selection of a laparoscopic approach in general should be followed. Contraindications include patients with acute intraperitoneal infection process and uncorrected coagulopathy. Although previous abdominal surgery is not an absolute contraindication, significant peritoneal adhesions should be factored into the decisionmaking process, which should be made on a case-by-case basis. Obesity is not, in itself, a contraindication to the laparoscopic approach; however, difficulty may be



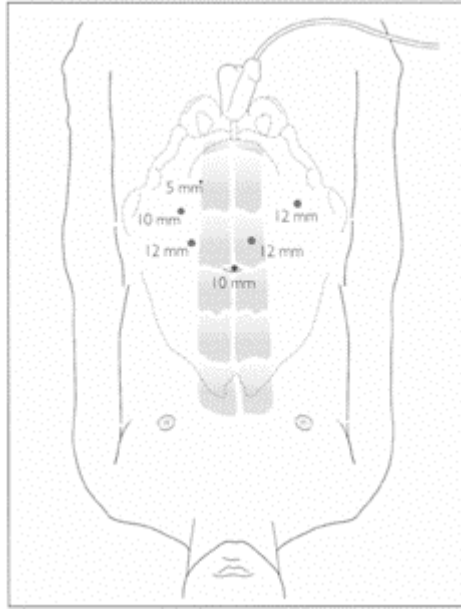
encountered during instrument manipulation, bowel mobilization, and while constructing an ileal conduit through the thicker abdominal wall.

### **Preoperative patient assessment and preparation**

The preoperative assessment for patients undergoing laparoscopic urinary diversion is similar to that for the open surgery. In brief, patients undergo a complete physical examination, routine blood tests (complete blood count, renal panel, alkaline phosphatase, liver function tests, and calcium), and radiographic testing to rule out metastatic disease. On the day prior to surgery, the bowel is prepared mechanically using 4 liters of GoLYTLEY, and chemically with neomycin and metronidazole. Broad-spectrum intravenous antibiotics and subcutaneous low-molecular-weight heparin (2500 units) are given prior to surgery.

### **Port placement**

Laparoscopic cystectomy, discussed elsewhere in this book, precedes the urinary diversion. The same five-port transperitoneal configuration is employed for both procedures, with one additional port in the left iliac fossa for the laparoscopic bowel work (Figure 51.1). A primary 10 mm port is placed at the umbilicus for the 0° laparoscope. Four secondary ports are placed under visualization: a 12 mm port to the left of the umbilicus, lateral to the rectus muscle, and two 10 mm ports in the left and right lower quadrants, approximately 2 fingerbreadths to the ipsilateral anterior superior iliac spines. In the case of an ileal conduit, another 12 mm port is placed at the preselected stoma site in the right rectus muscle; otherwise, this 12 mm port is placed at the lateral border of the rectus



**Figure 51.1** Transperitoneal six-port approach.

muscle, approximately 2 fingerbreadths caudal to the umbilicus. Finally, a 5 mm port is placed in the midline infraumbilical location, approximately 2 fingerbreadths cephalad to the symphysis pubis.

It is important to note that during the initial bowel manipulation (ileal segment isolation, ileal-ileal anastomosis) the laparoscope is inserted through the left lateral port while the surgeon works through the midline infraumbilical and the pararectal ports. If an ileal conduit is selected, this same triangular port configuration is used for the ureterointestinal anastomosis. However, if a continent reservoir is to be performed, the laparoscope is moved back to the umbilical port upon completion of bowel detubularization.

### **Laparoscopic ileal conduit**

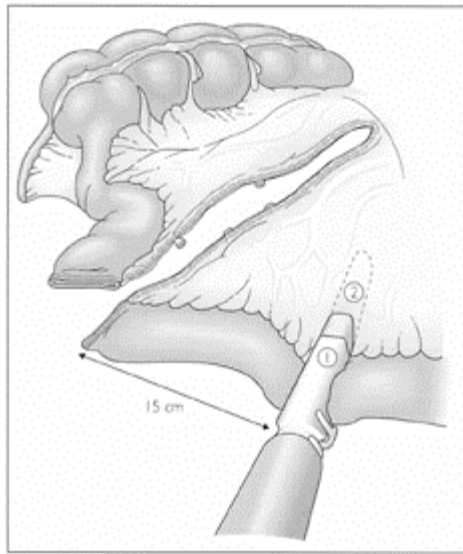
#### *Ileal conduit creation*

After the cystectomy and pelvic lymphadenectomy are completed, attention is focused on the urinary diversion. When an ileal conduit is selected for urinary diversion, a 15–20 cm segment of ileum is identified 20 cm away from the ileocecal junction. All bowel manipulations are performed completely intracorporeally.<sup>13,14</sup> In this manner, division of the selected segment of bowel and mesentery is performed using the EndoGIA stapler. Staple heights of 3.5 mm are used for bowel and 2 mm or 2.5 mm (vascular load) for the

mesentery. Two firings are used to complete the distal mesenteric division and one firing is used to complete the proximal division (Figure 51.2). As in open surgery, care is taken not to compromise the main mesenteric vessels feeding the conduit. Ileoileal continuity is re-established by creating a generous side-to-side anastomosis with two sequential firings of the Endo-GIA stapler. The open ileal ends are closed with two transverse firings of the Endo-GIA stapler. The mesenteric window is closed with 3–0 silk sutures. The distal end of the conduit is exteriorized through the preselected stoma site at the rectus muscle and an end-ileal stoma is fashioned using conventional techniques.

#### *Ureteroileal anastomosis*

Technical difficulty in performing laparoscopic freehand suturing was the main reason why the initial reports of laparoscopic ileal conduit urinary diversion employed conventional open techniques to perform the ureteroileal anastomosis. In these early 1990s reports, ureteral reimplantation was performed extracorporeally through either a minilaparotomy incision or by delivering the ends of the conduit and both ureters outside the abdomen through an



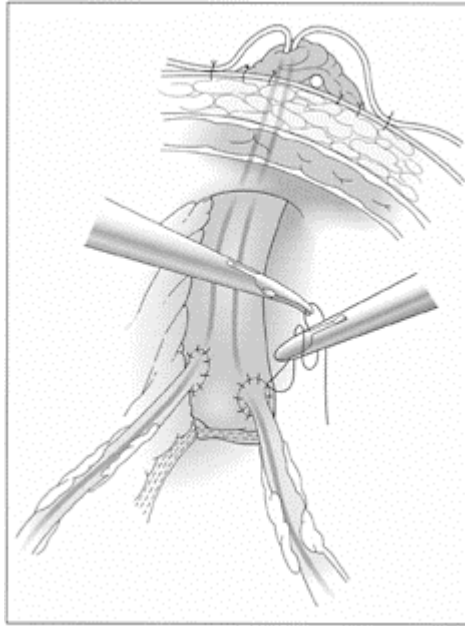
**Figure 51.2** Division of the isolated bowel segment and mesentery is performed with serial firings of the Endo-GIA stapler.

enlarged port-site incision.<sup>2,3</sup> In our view, such an extracorporeal anastomosis through a limited incision, as described, may create problems as regards tissue orientation and positional distortion.<sup>13</sup> Moreover, it may be difficult or even impossible to extract the

ileum and the ureters to the skin level in obese patients. One decade later, with advances in intracorporeal free-hand suturing, Gill et al reported the initial two cases of laparoscopic ileal conduit where the ureterointestinal anastomosis was performed completely intracorporeally.<sup>4</sup> In this technique, a 90 cm, 7F single-J stent is grasped with a laparoscopic right-angle clamp and inserted into the conduit lumen. It is then used to tent the conduit wall at the desired site of ureteroileal anastomosis. Using an electrical J hook, a small ileotomy is created and the stent is delivered into the abdominal cavity. The ureteral rim is freshened and spatulated. A 4–0 Vicryl (RB-1 needle) stitch is placed outside-in at the apex of the ureteral spatulation and is anchored to the desired site of the ileotomy. A running suture is then performed to approximate 80% of the posterior (far) wall and the J stent is fed into the ureter up to the renal pelvis. The remainder of the posterior wall anastomosis is completed. The anterior (near) wall is sutured in a running fashion with a second 4–0 suture to complete the anastomosis. The contralateral ureteral anastomosis is performed in a similar manner (Figure 51.3).

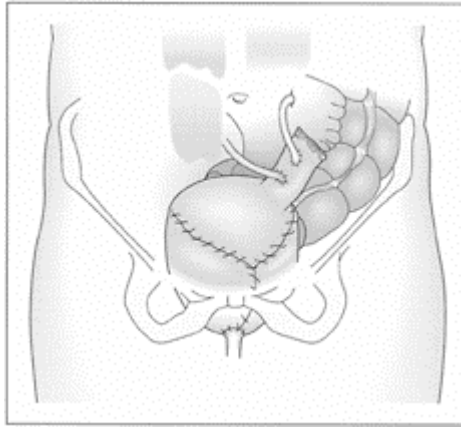
### **Laparoscopic orthotopic neobladder**

Following cystectomy and lymphadenectomy, a 65 cm ileal segment is selected and isolated in a similar manner as described above for the ileal conduit.<sup>4,15</sup> Bowel segment length is precisely measured by inserting a malleable footruler into the abdomen through a 12 mm port. The proximal 10–15 cm of the excluded ileal segment is reserved for the isoperistaltic Studer limb of the neobladder. The remaining length of the ileal segment is detubularized along its antimesenteric border using endoshears with electro cautery or the harmonic scalpel. The posterior wall of the neobladder is created by continuous intracorporeal suturing of adjacent edges of the U-shaped ileal segment using 2–0 Vicryl suture on a CT-1 needle.<sup>4,15</sup> The segment is then brought into the pelvis, avoiding any undue tension or torsion of the mesentery. The previously confirmed most-dependent portion of the ileal segment is selected for urethroileal (neobladder) anastomosis. A running circumferential suture is performed using 2–0 Vicryl on a UR-6 needle. Prior to completing the anastomosis, a 22F silicone Foley catheter is inserted per urethra. In female patients, two 90 cm single-J stents are inserted via the external urethral meatus alongside the Foley catheter and delivered into the neobladder. In the male,



**Figure 51.3** Ileal conduit urinary diversion. The distal end of the ileal loop secured to the skin using the standard technique. Stented is exteriorized through the preselected stoma site and is bilateral ureteroileal anastomoses are completed.

these two stents are inserted through the right lateral port into the neobladder. The anterior wall of the neobladder is folded forward and the free edges are sutured to achieve a spherical configuration. Prior to completion of the neobladder suturing, a 5 cm incision is performed in the anterior wall of the Studer limb and the stents are delivered through it. Two small ileotomies are created at the side of the Studer limb, and one ureter is pulled inside the Studer limb through each ileotomy. The ureters are then freshened and spatulated. A full-thickness anchoring stitch affixes the edge of the ureter to the apex of the ileotomy. The single-J stent is delivered up to the renal pelvis and two additional stitches are placed between the ureter and the ileum wall. Finally, the anterior wall of the Studer limb is closed with a running suture (Figure 51.4). All suturing and knot tying is performed intracorporeally using a freehand laparoscopic technique.<sup>4,15</sup> The neobladder is irrigated through the Foley catheter and any obvious sites of leakage are specifically repaired with figure-of-eight stitches. A suprapubic catheter is inserted into the neobladder through the midline port-site incision.



**Figure 51.4** Orthotopic neobladder urinary diversion. After isolation of the ileal segment and detubularization of the distal portion, the posterior plate is created and urethroileal anastomosis is completed using a running suture. The anterior wall of the neobladder is folded to achieve a spherical configuration of the neobladder.

#### **Laparoscopic rectal sigmoid (Mainz II) pouch**

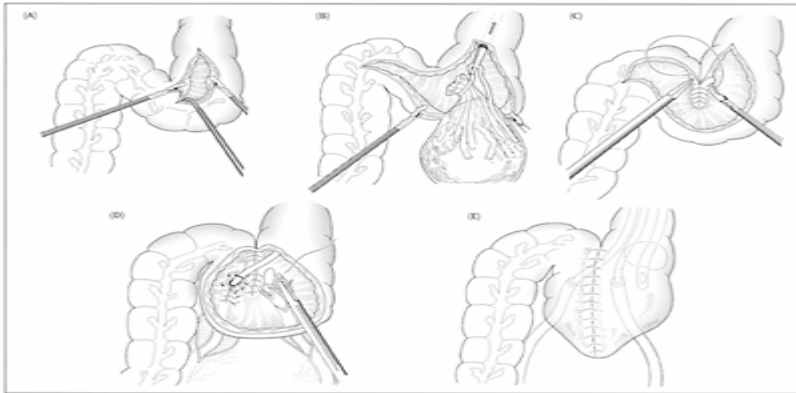
Türk and colleagues were the first to report a laparoscopic rectal sigmoid pouch.<sup>16</sup> This rectal sphincter-based continent type of urinary diversion was successfully performed in 5 patients completely intracorporeally. Upon completion of cystectomy, the rectosigmoid colon was incised open along its antimesenteric border with a hook electrocautery. This incision was then extended for 10 cm, respectively, proximally and distally from the rectosigmoid junction. The adjacent posterior walls of the rectum and sigmoid were anastomosed side to side with absorbable running suture, forming the posterior wall of the pouch. Subsequently, the mobilized ureters were brought into the pouch and sutured to the pouch plate in a pre-prepared 3 cm submucosal bed. Single-J 8F stents were inserted through the anus into the pouch and then passed up to the renal pelvis. A submucosal tunnel was formed by suturing the mucosa over the ureters. Finally, the anterior wall of the pouch was closed with a running suture of 3–0 Vicryl. The pouch was drained transanally with a Nelaton catheter. In the female patient the specimen was extracted intact through the vagina, while in the male patient the specimen was placed in an endoscopic bag and extracted transanally.

### Laparoscopic-assisted reconstruction of pouch/enterocystoplasty

Alternatively, during laparoscopic procedures, bowel manipulation as well as construction of complex enteric pouches or enterocystoplasty can be performed extracorporeally (Figure 51.5). This technique is described in Chapter 20. Generally, a 2–5 cm incision is performed to exteriorize the preselected bowel segment. Several advantages can accrue:

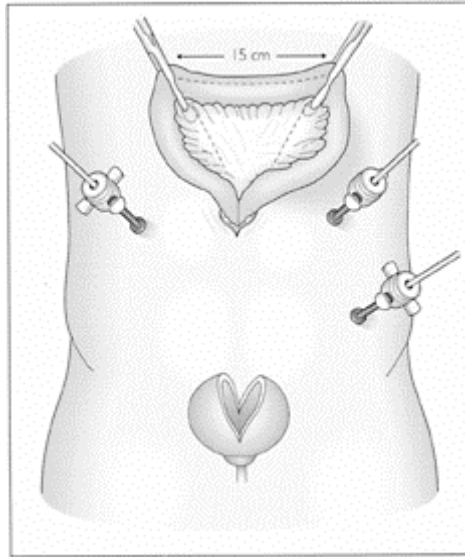
- bowel mesentery can be precisely incised after ensuring good vascularity using transillumination
- side-to-side bowel anastomosis can be performed rapidly
- contamination of the abdominal cavity can be prevented during detubularization of the loop
- overall this approach allows considerable savings in operative times.<sup>17</sup>

Recently, we reported a laparoscopic-assisted continent Indiana pouch urinary diversion in a patient with muscle invasive bladder cancer.<sup>4</sup> Due to urethral involvement, orthotopic diversion was contraindicated in this case. The pouch and continent catheterizable ileal limb were created extracorporeally by standard open techniques after the selected ileocecal segment was extruded through a 2–3 cm extension of the right pararectal port incision. Subsequently, the bowel was reinserted into the abdomen, and the bilateral uretero-ileal anastomoses were created intracorporeally by freehand laparoscopic techniques.



**Figure 51.5** Construction of a rectosigmoid pouch: (A) the rectosigmoid is incised at the antimesentery border; (B) the cystectomy specimen is extracted through the rectum; (C) the posterior wall is anastomosed side to side; (D) the ureters are implanted via a

submucosal posterior tunnel; (E) the ureters are stented with ureteral catheters and the pouch is drained with a 26F Nelaton catheter. The anterior wall of the pouch is closed.



**Figure 51.6** During laparoscopic procedures, bowel work can be performed through an extended port-site incision.

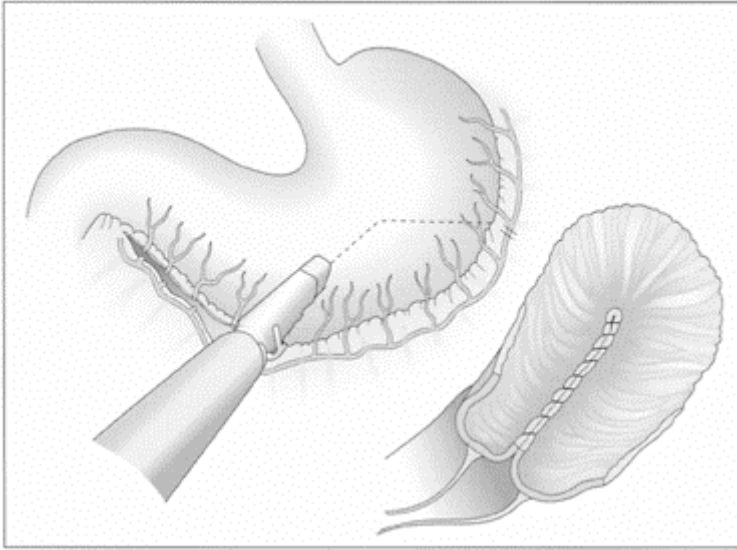
### Laparoscopic gastroileal neobladder

Although demanding more complex gastrointestinal resection, the combination of bowel and stomach to create a pouch may have metabolic advantages compared to the use of intestinal segments alone. The tendency to metabolic acidosis when ileum or colon is used in urinary reconstruction can be counterbalanced by the combined use of stomach, due to its tendency towards metabolic alkalosis. Thus, metabolic neutrality may be achieved in highly selected cases. These composite reservoirs may be employed judiciously in the setting of metabolic acidosis, short bowel syndrome, and renal failure. To date, no clinical reports of laparoscopic use of stomach for urinary diversion have been reported. Experimentally, Carvalhal et al described the construction of a gastroileal composite reservoir in a porcine model.<sup>18</sup> Briefly, the surgical steps were:

1. gastric mobilization and right gastroepiploic pedicle dissection



2. wedge resection of the greater curvature (8–12 cm× 4 cm) with Endo-GIA stapler (Figure 51.7)
3. isolation of a 20 cm ileal segment
4. stapled restoration of ileoileal continuity
5. cystectomy and ureteral dissection
6. construction of the composite gastrointestinal plate (gastric patch and U-shaped ileum) with freehand laparoscopic suturing



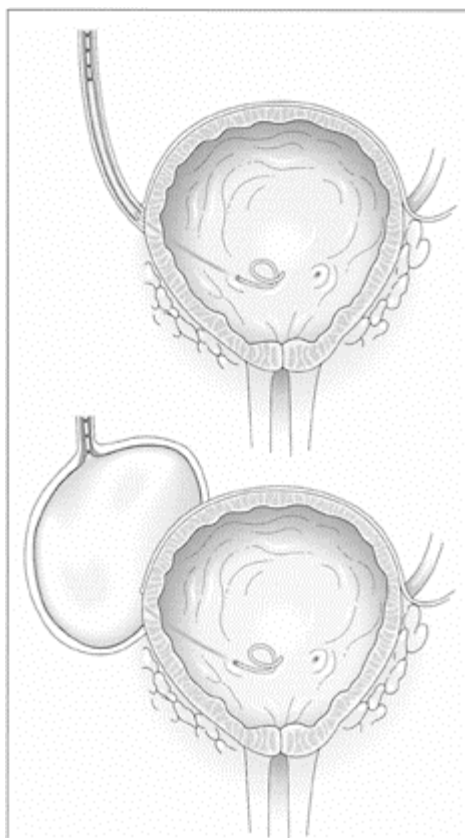
**Figure 51.7** Laparoscopic wedge resection of the greater curvature of the stomach is performed to create a composite pouch with an ileal segment.

7. urethroileal anastomosis
8. bilateral reimplantation into the gastric patch
9. closure of the composite plate in a spherical manner.

Intracorporeal laparoscopic freehand suturing was employed exclusively. The complexity of the procedure explains the long mean operative time of 7.1 hours in this experimental model.

### **Laparoscopic ureterocystoplasty using balloon-expanded normal ureter**

Despite all the technical advances with minimally invasive use of intestine for urinary diversion, the problems inherent to the contact of urine with bowel mucosa have not been overcome and continue to be a source of morbidity. Perhaps the ureter, with its transitional epithelium, may be the ideal tissue for bladder augmentation or replacement. However, the use of ureteral tissue for this purpose is limited to the rare patient with a megaureter subtending a nonfunctional kidney. The concept of ureteral tissue expansion was initially proposed by Hensle and colleagues.<sup>19</sup> Recently, we have completed an experimental study wherein a balloon device was used to expand the normal ureter.<sup>20</sup> This balloon (Microvasive, Natick, Massachusetts) is mounted in a dual-channel catheter: one for balloon inflation and the other for proximal nephrostomy drainage. Using a porcine model, a percutaneous renal tract was dilated, followed by the passage of the expansion balloon device. The balloon was then manipulated antegradely into the juxtavesical ureter (Figure 51.8). The ureteral balloon was gradually inflated over a 2–3 week period by instillation of dilute contrast solution. The inflation was performed without anesthesia, while the animal was eating. The mean daily inflation volume was 1.8, 5.5, 9.5, and 16.1 ml/day respectively in the first, second, third and final week. Total balloon volumes averaged 12.9, 60.3 and 171.8 ml respectively, at 1, 2, and 3 weeks. After completion of ureteral balloon expansion, laparoscopic ureterocystoplasty was performed. Over a follow-up ranging from 15 days to 3 months, a mean augmented bladder capacity of  $574 \pm 221.3$  ml was achieved. In the future, such expanded ureteral tissue may be successfully used to augment or replace the bladder using minimally invasive techniques.



**Figure 51.8** A balloon catheter is inserted antegradely into the juxtavesical ureter to gradually expand the normal ureter.

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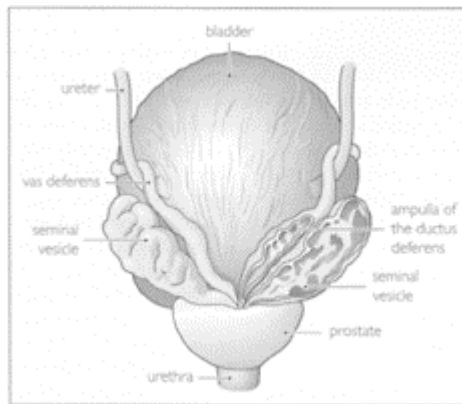
## 52

### Seminal vesicle disease

Salvatore Micali and Pierluigi Bove

#### Embryology, anatomy, and physiology

The seminal vesicles (SV) are two elongated, convoluted glands lying between the fundus of the bladder and the rectum, just above the prostate (Figure 52.1). Each SV is pyramidal in form, the broad end being directed cephalad and posteriolaterally. It is usually about 7.5 cm long, but varies in size, not only in different individuals but also in the same individual on the two sides. The anterior surface is in contact with the fundus of the bladder, extending from near the termination of the ureter to the base of the prostate. The posterior surface rests upon the rectum, from which it is separated by the rectovesical fascia. The upper extremities of the two vesicles diverge from each other, are in close relation with the ductus deferentes and the terminations of the ureters, and are partly covered by peritoneum. The lower extremities are pointed, and converge



**Figure 52.1** Seminal vesicle and its relationship to bladder, ureter, vas deferens, and prostate.

toward the base of the prostate, where each joins with the corresponding ductus deferens to form the ejaculatory duct. Along the medial margin of each vesicle runs the ampulla of the ductus deferens. When uncoiled, the tube is about the diameter of a quill, and varies

in length from 10 to 15 cm: it ends posteriorly in a cul-de-sac; its anterior extremity becomes constricted into a narrow straight duct, which joins with the corresponding ductus deferens to form the ejaculatory duct. Blood supply for the SV is provided by the vesicod deferential arteries, the inferior vesical arteries and the superior and middle rectal arteries. Venous drainage is guaranteed by a rich venous plexus located posteriorly, which drains into the vesicod deferential vein and into the inferior vesical plexus. Lymphatics drain into the hypogastric lymph nodes. Adrenergic innervation is provided by nerve branches arising from the hypogastric plexus.

The SV embryologically develop as saccular outgrowths from the mesonephric duct. Between weeks 4 and 7 of gestation the ureteral bud sprouts from the caudal end of the mesonephric duct. Cranial growth of the ureteral bud toward the metanephric blastema stimulates renal development. In week 13 of gestation the SV sprout from the mesonephric duct in a location more cephalad than the ureteral bud. Additional structures arising from the mesonephric duct system include the vas deferens, the ejaculatory duct and the lower two-thirds of the epididymis.

Histologically, the SV are composed of an external layer of fibrous connective tissue, a middle layer of smooth muscle, and an inner mucosal layer that includes luminal epithelial cells and a variably prominent basal cell population. The SV contain a dense, and alkaline (pH 7.2–7.8), yellowish substance rich in proteins, fructose, sorbitol, citric acid, and prostaglandins E, A, B, and F. Among these components a coagulative factor is present. This SV substance is secreted by the epithelium, under the stimulation of male hormones, and represents the main component (50–80%) of the semen. It promotes sperm motility, providing for their nourishment and survival.

## **Clinical examination, laboratory tests, and diagnostic imaging**

### *Physical examination*

Physical examination may demonstrate an indurated, tender epididymis and ductus deferens, which are evidence of chronic epididymitis or obstruction. Digital rectal examination (DRE) and seminal vesiculography have been the main aids for detecting pathologic conditions of the SV. The SV are located too cephalad to be palpated entirely. The area located just above the prostate may feel enlarged and relatively tender if there is an SV cyst or hard and fixed when neoplastic extension occurs.

### *Laboratory test*

Laboratory evaluation may reveal positive culture of prostatic secretions or ejaculate and elevated serologic markers of chronic infection, such as complement C3 or ceruloplasmin. On analysis of the semen, a low quantity of semen and the absence of both fructose and a liquefaction process are evidence of SV agenesis or ejaculatory duct obstruction. A serum testosterone is required to rule out hypogonadism, and the next step, in traditional evaluation of ejaculatory duct obstruction, is the testis biopsy, which should reveal normal spermatogenesis.

### *Ultrasonography*

Transrectal ultrasonography (TRUS) provides fine crosssectional images of the SV. Above the prostate, the SV appear as two symmetric, elongated, and convoluted cysts, hypoechoic if compared to the prostatic parenchyma. At the medial extremity of each SV the deferential ampullae can be identified (Figure 52.2). Contemporary ultrasound devices permit clear delineation of the SV components: the SV wall appears hyperechoic compared to the hypoechoic fluid spaces. The SV are usually considered to be dilated when the axial diameter is  $>1.5$  cm on TRUS; this finding is suggestive of ejaculatory duct obstruction.<sup>1-3</sup>

TRUS allows identification of both congenital and acquired disorders of the SV and, more recently, has become the most commonly used noninvasive technique for investigating the male reproductive tract. It plays a critical role in both the diagnosis and treatment of disorders causing complete or partial obstruction of the seminal duct system.

Cysts are the most frequently observed SV anomalies. Ultrasonography shows cysts as hypoechoic masses (Figure 52.3) developing in or outside the SV that can displace the bladder or surrounding structures.<sup>4</sup> TRUS is useful to guide transrectal or transperineal needle aspiration, which may transiently relieve symptoms and allow the instillation of contrast material to establish the correct diagnosis. Simple cyst drainage is associated with the risk of recurrence, return of symptoms, and possible infection.<sup>5</sup> Solid malignancies generally appear as isoechoic lesions when compared to the normal prostatic ultrasound pattern, but relatively more echogenic than the normal SV echostructure. There is no evidence that clearly distinguishes benign from malignant or primary from secondary diseases of the SV except for a more frequent unilaterality of primary lesions.

### *Computer tomography*

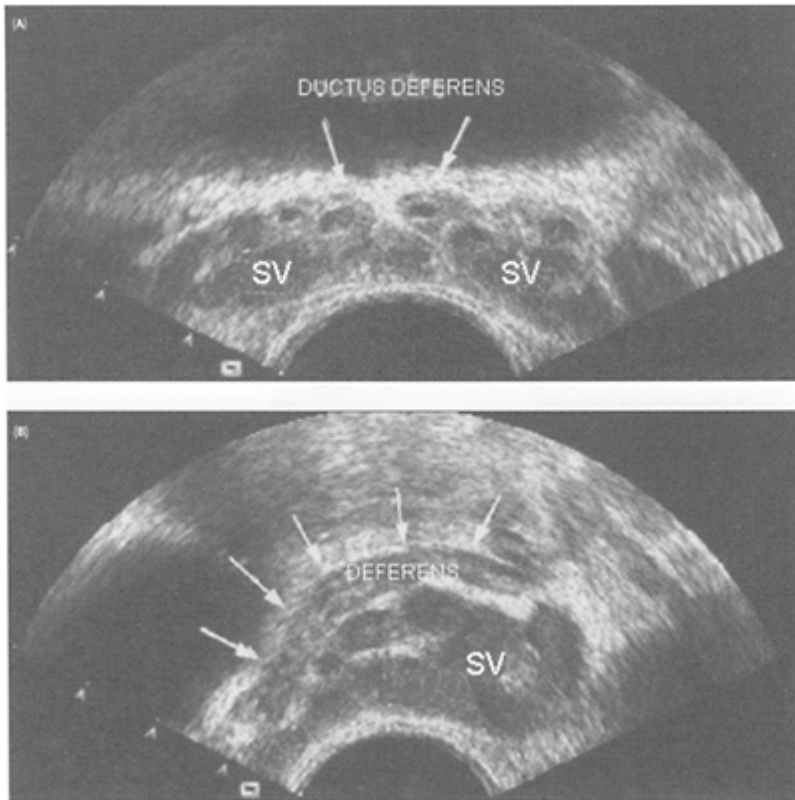
The SV have the same density as muscular tissue. Computed tomography (CT) has been used to identify congenital anomalies of the SV and this remains its best use.

Tumors located in the SV are easily detected by the CT as masses with an attenuation number higher than the normal SV wall. CT does not allow one to distinguish either malignant tumors from benign masses or primary from secondary lesions, although a malignancy originating in the prostate or the rectum can be inferred when an invasion of the tissue layers is present.<sup>6</sup>

### *Magnetic resonance imaging*

Magnetic resonance imaging (MRI) is not more sensitive than TRUS or CT in the detection of SV diseases, although MRI features (T1–T2 weighted images) maybe more precise in diagnosing a cystic lesion and in staging a solid pelvic tumor. SV cysts are similar to the simple cysts present in other body areas, when scanned with MRI. In this case T1-weighted images show unilocular cysts with a thin wall and well-defined margins.<sup>7,8</sup> At present there is little information available on MRI accuracy in the study of SV tumors. Patients with symptoms or positive DRE suggestive of anomalies or a pelvic mass should undergo a TRUS as first examination (Figure 52.4). If a solid mass is found, a transperineal ultrasound-guided biopsy will confirm the presence of a

malignancy, and CT is necessary. The MRI is helpful only in confirming the hemorrhagic nature of a mass or in better defining the neoplastic extension to adjacent pelvic organs. Endorectal MR imaging may be helpful to assess the relationships between the proximal prostatic urethra and the posterior wall of the ejaculatory duct. This is important information when transurethral resection of the ejaculatory duct is planned.<sup>9</sup>



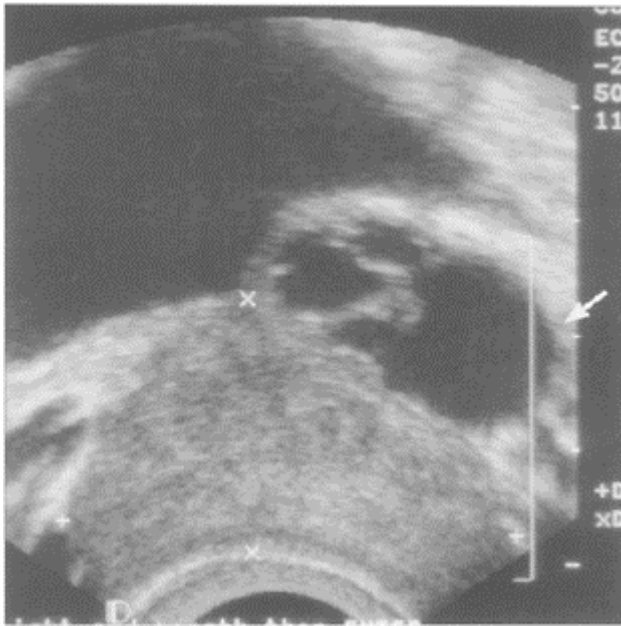
**Figure 52.2** (A) Transverse ultrasonic image of the seminal vesicles (SV) and ductus deferens. (B) Longitudinal ultrasonic image of SV and ductus deferens.

#### *Seminal vesiculography*

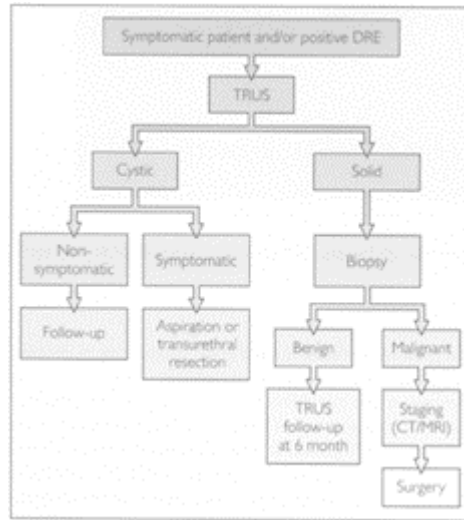
Contrast examination of the seminal vesicles can be performed in different modalities with different and uncertain results. The transurethral approach consists of a direct injection of contrast medium into the ejaculatory duct, utilizing a curved tip of a 5F ureteral catheter.<sup>20</sup> This approach is time consuming and requires experience. A second



way to visualize the SV is the antegrade technique after surgical exposure of the vas deferens at the scrotal level. A 30-gauge lymphangiogram needle allows the injection of the contrast medium. It has a good success rate in defining vas deferens obstructions in infertile men. Sometimes stenosis of the vas deferens can develop at the puncture site.<sup>10-12</sup> Transperineal or transrectal direct puncture of the SV under TRUS guidance is recommended only in selected cases.<sup>10,13</sup> With injection of contrast media and methylene blue into dilated SV or cysts, a clear picture of the anatomy can be provided; moreover, methylene blue facilitates visualization of the effluxing dye mixture during transurethral resection.<sup>14</sup> Vasograms are considered suggestive of ejaculatory duct obstruction when the following are seen:



**Figure 52.3** Seminal vesicle cysts are the most common SV anomaly. Ultrasound images delineate an SV cyst as a hypoechoic mass.

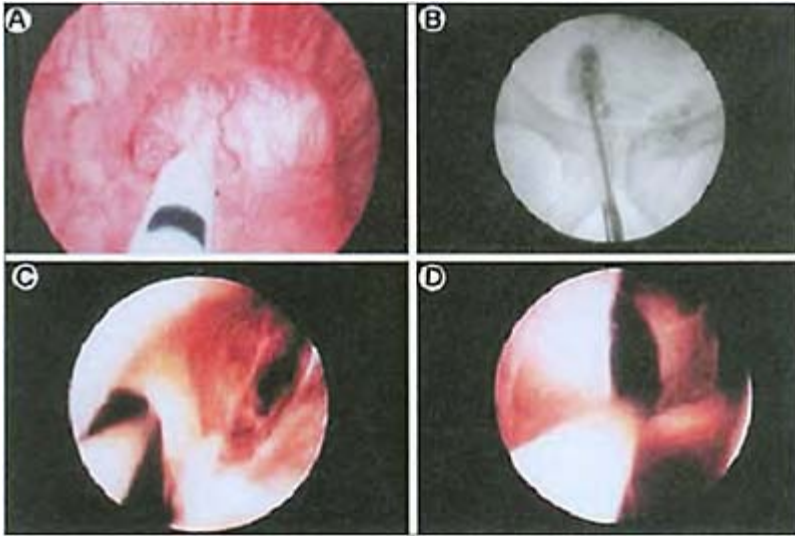


**Figure 52.4** Flow chart delineating the work-up positive digital rectal examination with perineal discomfort.

- midline cysts communicating with the SV and vas
- SV dilatation (greater than 6 cm long and greater than 2 cm wide)<sup>15,16</sup>
- narrowing of the ejaculatory ducts<sup>17,18</sup>
- distortion or asymmetry of normal ejaculatory duct anatomy.<sup>17,18</sup>

### *Endoscopy*

Endoscopy of an SV was first reported in 1996 using exvivo specimens obtained at radical cystectomy and prostatectomy<sup>19</sup>. In 1997 the feasibility of in-vivo transurethral endoscopy of the SV was demonstrated.<sup>20</sup> The identification of the ejaculatory duct orifice can be achieved by injection of dye from a cannulated vas deferens. However, insertion of a guide wire into the ejaculatory ducts can be difficult because the orifices are positioned on either side of the verumontanum. Under direct vision, a curved tip of a 5F ureteral catheter allows an easier passage of a guide wire (0.032 inch) into the ejaculatory duct. The catheter is then advanced over the guide wire to the ampulla of the vas deferens (Figure 52.5A-D) and a 6F semirigid ureteroscope is passed, through a 22 cystoscopy sheath, over the guide wire (Figure 52.5D). The endoscope may be



**Figure 52.5** Endoscopy of the seminal vesicle. (A) Under direct vision a curved tip 5F ureteral catheter cannulated the ejaculatory duct on each side of the verumontanum. (B) Seminal vesicogram is performed by injection of 1–3 ml of contrast agent under fluoroscopic control. (C) A guide wire (0.032 inch) is passed through the 5F ureteral catheter. The ureteral catheter is removed and the guide wire is left in place. (D) A 6F semirigid ureterscope is passed, through a 22F cystoscopic sheath, over the guide wire. The endoscope is advanced to visualize the SV lumen.

advanced to visualize the SV lumen. This technique makes possible new diagnostic and therapeutic approaches to malignant and benign disorders of the seminal vesicle associated with male infertility.

Cystoscopy may identify an absent ipsilateral hemitrigone, an intravesical cyst protrusion, and any other anatomic abnormalities of the bladder. Concurrent bladder pathology should be ruled out in any patient presenting with irritative voiding symptoms and/or hematuria.

## Seminal vesicle diseases

### *Congenital lesions*

Congenital SV lesions are uncommon but currently are being detected more frequently with the use of sectional imaging procedures. The most common congenital anomalies are SV agenesis and SV cysts.

### Seminal vesicles agenesis

Unilateral agenesis of SV is not rare, with a reported incidence between 0.6% and 1%. It can be associated with unilateral agenesis of the vas deferens or with unilateral renal anomalies. Bilateral agenesis of SV is frequently associated with bilateral absence of the vasa. This condition is observed in 60–80% of men with cystic fibrosis.<sup>21,22</sup> Seminal vesicle agenesis does not require any treatment.

### Cysts

The most common SV anomalies are congenital cysts. In two-thirds of the cases this condition is associated with renal dysplasia or renal agenesis and an ectopic ureter opening into the seminal vesicle.<sup>23</sup> Some authors describe an association of this disorder with infertility,<sup>24</sup> hemospermia,<sup>25,26</sup> and genitourinary infections.<sup>27–29</sup> Acquired cysts may be due to genitourinary infections, prostate resection, or ejaculatory duct lithiasis.<sup>30</sup> The mechanism of cyst formation is thought to be the buildup of SV fluid due to an abnormal or obliterated ejaculatory duct.<sup>31</sup> The diagnosis of this condition is usually made in the third to fifth decades of life.<sup>5,27,28,32</sup> Symptoms may develop due to irritation of adjacent organs by the enlarged and inflamed SV cyst. Bladder irritation causes urgency, frequency, dysuria, and hematuria. Cyst distention may cause perineal or suprapubic pain, hematospermia, postcoital discomfort, or painful defecation.<sup>5,27,32–34</sup> The seminal vesicle cyst can be responsible for vesiculitis, abscess, and stone formation.

Treatment is reserved for symptomatic cases. Incidentally discovered SV cysts that do not cause pain or functional impairment should be followed without intervention. However, there are anecdotal reports of primary malignancies arising from these cysts.<sup>35</sup>

TRUS is useful to guide transrectal or transperineal aspiration that may transiently relieve symptoms, but the preferred treatment of patients with symptomatic SV cysts is seminal vesiculectomy.

### *Acquired lesions*

Cystic pathology represents the most frequently acquired lesion, SV tumors being an extremely rare finding. Neoplasm of the SV may be benign or malignant and primary or secondary to a pelvic tumor. The most common benign tumors are the cystadenoma and the papillary adenoma. Reported primary SV tumors include a spectrum of carcinoma, mesenchymal tumors, and an uncommon group of neoplasms containing a mixture of both epithelial and stromal components. Because secondary involvement of the SV by prostate cancer is relatively common, strict criteria must be applied to diagnose primary

SV carcinoma (the neoplasm must be a papillary or an anaplastic carcinoma localized primarily within the SV, and there should be no other primary carcinoma in the region).<sup>36</sup>

### Benign tumors

**Cystoadenoma.** Cystoadenoma occurs in patients with mean age of about 50 years old. Generally, it involves a single seminal vesicle. The clinical picture is characterized by a retrovesical cystic tumor that may cause nonspecific symptoms or it may be discovered incidentally at clinical examination or at autopsy.<sup>37</sup> The differential diagnosis encompasses all space-occupying lesions of the retrovesical space. Complete surgical removal of the tumor and, if necessary, vesiculectomy or vesiculoprostatectomy is the only definitive treatment.<sup>37</sup>

### Malignant tumors

**Adenocarcinoma.** Although rare, adenocarcinoma is the most common primary neoplasm of the seminal vesicles. The mean age at the diagnosis is 62 years old; most patients present with urinary outlet obstructive symptoms. Physical examination typically reveals a palpable, nontender mass superior to, or confluent with, the prostate. The prognosis is poor, and because of the small number of cases, there is no consensus on management; local excision or radical surgery, combined with hormonal therapy, radiation therapy or chemotherapy, have all been utilized.

### *Obstruction of the seminal duct system*

Ejaculatory duct obstruction is a pathologic condition diagnosed in 7–14% of infertile men; it is a moderately rare and treatable cause of male infertility.<sup>38</sup> The pathologies causing complete or partial obstruction of the seminal duct system can manifest with infertility, low ejaculate volume, hematospermia, perineal or testicular pain, painful ejaculation, and urinary obstruction.<sup>3,17</sup> In such patients a small ejaculate volume with low pH and absent fructose but with palpable vasa deferentia, and often some epididymal thickening, are virtually pathognomonic of a bilateral ejaculatory duct obstruction.

Ejaculatory duct obstruction may be a congenital or acquired pathology. Atresia or stenosis of the ejaculatory ducts and utricular, müllerian, and wolffian duct cysts represent the most common congenital causes. Acquired causes may be secondary to trauma, or infectious or inflammatory diseases of the genitourinary tract.<sup>17,39</sup>

Transurethral resection of the ejaculatory duct is the standard treatment for these conditions but with variable results.

### Treatments

In the case of SV lesions with no evidence of local extension and without any malignant characteristics on histopathologic examination, treatments depend only on the presence of symptoms. In the absence of symptoms, strict follow-up is reasonable, repeating DRE and TRUS to determine any evolution of the lesion. If the mass grows or causes any

symptoms, a partial or simple vesiculectomy is necessary. Alternatives are completely different in the case of a large, solid mass with histologic evidence of malignancy. However, with so few cases reported it is impossible to make conclusive recommendations regarding optimal therapy. Radical excision, generally including cystoprostatectomy with pelvic lymph node dissection, is the treatment of choice, except for extremely small tumors. There is no known effective chemotherapy.

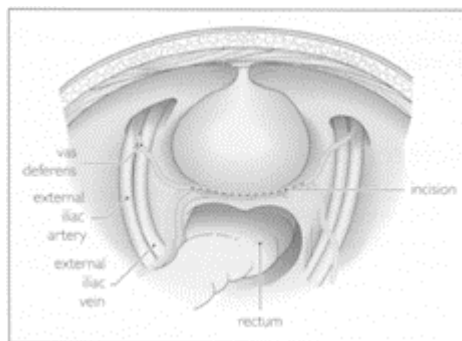
It is crucial to identify ejaculatory duct obstruction to determine the appropriate treatment for patients with correctable defects. Surgically correctable causes are lesions involving the distal two-thirds of the ejaculatory duct, including ejaculatory duct cysts, calculi, fibrosis, and calcifications. Agenesis, obstruction, or occlusion of the ductal system above this level is not currently correctable.<sup>40</sup>

### *Medical and radio logic treatment*

TRUS is useful for transrectal or transperineal aspiration of SV cysts; it should be the treatment of choice to transiently relieve symptoms. In the case of lesion recurrence, a direct puncture allows the instillation of a sclerosant such as a tetracycline.

### *Endoscopic treatment*

A preoperative TRUS is necessary to determine the precise location of the cyst and its distance from the bladder neck and urethral mucosa. Intraoperative vasography (see Seminal vesiculography section) is performed to assess the ejaculatory duct obstruction and to facilitate visualization of the ejaculatory ducts. With the patient in the lithotomy position, a standard 24F resectoscope is advanced as far as the prostatic urethra. An electrified loop is used to resect the tissue space using cutting current. Cautery is used with caution to avoid potential scarring of the open duct. The techniques of transurethral resection vary from unroofing the midline cyst to deep aggressive resection into the SV until injected methylene blue gushes out. If the cyst is adja-



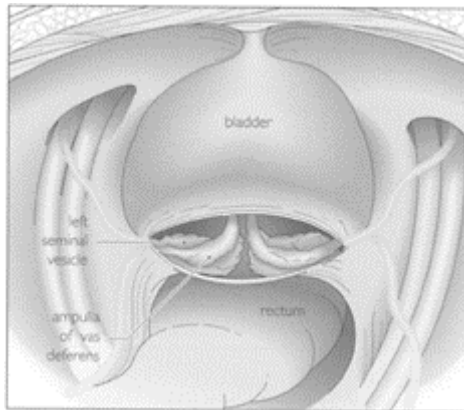
**Figure 52.6** Line of incision of the peritoneum overlying the SV at the level of the vas deferens.

cent to the prostate, it is possible to marsupialize the cavity by a deep transurethral prostate resection, just distal to the bladder neck at 5 and 7 o'clock.<sup>41–43</sup> Transurethral resection is facilitated by placing a gloved finger in the rectum to squeeze the SV.

Unfortunately, transurethral resection of the ejaculatory ducts or unroofing of intravesical cysts have met with limited success in the literature and in our experience. Potential complications from transurethral resection of ejaculatory ducts include rectal injury, external sphincter injury, bladder neck resection resulting in retrograde ejaculation, and secondary urinary reflux into the vas deferens.<sup>44–45</sup>

### *Laparoscopic treatment*

Laparoscopy has been advocated as an optimal minimally invasive technique for surgical treatment of seminal vesicle pathology.<sup>23,46,47</sup> Kavoussi et al in 1993 described the principles of laparoscopic surgery on normal SV in order to facilitate transperineal prostatectomy in patients with prostate cancer.<sup>46</sup> His technique is described as follows. A total of five ports are necessary: a 12 mm trocar in the umbilicus, a 10 mm trocar on each side lateral to the rectus muscle and just below the level of the umbilicus, and a 10 mm trocar in each lower quadrant, approximately 5 cm below the level of the upper trocars. A transverse incision is made through the anterior peritoneum overlying the rectovesical pouch (Figure 52.6). The peritoneum is teased bluntly off of the underlying tissues and, with minimal dissection in the midline, the ampullae of vasa deferentia on each side are identified (Figure 52.7). Each ampulla can



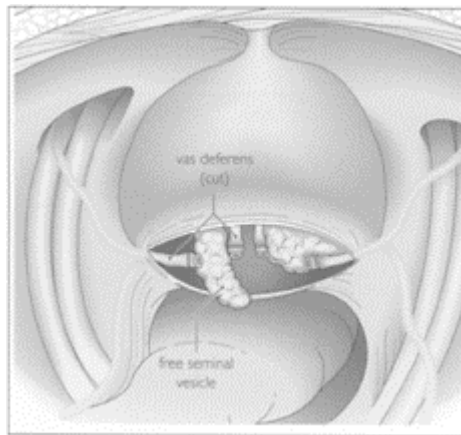
**Figure 52.7** After peritoneotomy, the peritoneum is gently dissected off the underlying tissues. Minimal dissection in the midline will expose the ampullae of the vasa deferentia on each side.

be now isolated, clipped, and transected. It is important to dissect in close proximity to the SV to avoid rectal or ureteral injury. At the bladder level the ureter lies just lateral and

posterior to the vas deferens. Working in a medial to lateral direction, the surface of each seminal vesicle is defined by blunt dissection and the artery to the SV may be isolated, clipped and transected (Figure 52.8). Gently grasping each SV and pulling medially makes it possible to dissect lateral attachments from the area of the neurovascular bundle. Avoid electrocautery in this area to prevent injury to the neurovascular bundles. Once the SV are freed, blunt dissection is used to push the rectum off of the posterior surface of the prostate.

A transperitoneal approach to treat SV cysts may be achieved through four laparoscopic ports.<sup>47,48</sup> After pneumoperitoneum is achieved, a 10 mm trocar is inserted into the umbilicus and the abdomen is examined with a 0° lens. A second 12 mm trocar is positioned in the midline 3 cm above the pubis. Two 5 mm trocars are introduced on either side lateral to the rectus abdominus muscle and a short distance below the umbilicus. The bladder is retracted anteriorly and the retrovesical peritoneum is incised transversely, facilitating SV cyst exposure. The cystic and dilated SV is dissected caudally to its junction with the prostate gland, where it is clipped and divided.

A partial vesiculectomy, consisting of cyst removal with preservation of the seminal vesicle remnant and the vas deferens, has been described.<sup>49</sup> It can be used in fertile men with an SV cyst with an unobstructed ejaculatory duct;



**Figure 52.8** The SV is isolated by dissection from medial to lateral via blunt dissection. The artery of the SV is localized laterally and controlled with either a harmonic scalpel or a clip applicator. Medial retraction of SV will separate it from the area of the neurovascular bundle.

preservation of both seminal tracts helps to ensure the maintenance of good semen parameters and decreases the risk of injury to the neurovascular bundles.



The growing interest in laparoscopic radical prostatectomy, performed with either a transperitoneal or an extraperitoneal approach, has permitted rapid improvement of these techniques, since the first step of transperitoneal laparoscopic prostatectomy is vesiculectomy. The laparoscopic approach to SV diseases seems to improve operative time and reduce morbidity.

### *Open surgical treatment*

In the past, operative surgical treatment has been accomplished via an open transvesical, transperineal, retroperitoneal, or posterior transcoccygeal approach.<sup>50,51</sup> Each technique can result in significant postoperative morbidity. Because of the deep location of the SV in the retrovesical space, open surgical access necessarily involves a large incision and extensive bladder mobilization or cystotomy. The morbidity of such open surgery is amplified because these patients are often young and active.

Today, the open surgical approach should be used only for large, solid pelvic masses.

### **Conclusion**

In conclusion, seminal vesicle diseases are rare clinical entities. Presenting symptoms are often vague and include perineal discomfort and voiding symptoms. The most common pathologic finding is an SV cyst. The best means of diagnosing SV disorders is transrectal ultrasound, and the best therapeutic approaches generally are laparoscopic procedures. Attention to clinical details and use of contemporary imaging modalities, coupled with minimally invasive treatment, have increased the awareness of SV disorders in the urologic community.

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## Complications of ureteroscopy and percutaneous renal surgery

Noah S Schenkman

### Introduction

Ureteropyeloscopy and percutaneous nephrolithotomy (PNL) have developed rapidly and have quickly achieved widespread acceptance over the past quarter century as part of a trend in minimally invasive surgery. With these procedures have come a new set of complications unique to endoscopic surgery. As technology has improved and the procedures have become routine among general urologists, overall complication rates have declined.

Most complication data on large retrospective series are instructive for the most significant complications. These complications are not missed because they are readily apparent to the surgeon at the time of the procedure or serious enough for a patient to report back to the physician in the early postoperative period. More subtle complications such as postoperative pain, colic, low-grade fevers, or minor urinary tract infection are often missed, especially in the era of outpatient procedures. In the past, when a 1–2 day stay was required, surgeons were more likely to directly observe these minor complaints. Lack of standardization among investigators in reporting the type and severity of complications leads to some difficulty in comparing results between different institutions. A true level of complications can be gleaned only from a standardized prospective investigation of patients undergoing ureteropyeloscopy and percutaneous nephrolithotomy.

### Ureteroscopy

#### *Brief review of procedure*

Ureteropyeloscopy is initiated with a complete cystoscopic examination and retrograde ureteropyelography of the affected side(s). A guide wire is passed into the ureter and advanced up to the renal pelvis. The cystoscope is withdrawn and the semirigid ureteroscope is placed alongside the guide wire into the ureter. If flexible ureteropyeloscopy is done, a second ‘working’ guide wire is passed up to the renal pelvis using a coaxial introducer system over the safety guide wire. The flexible ureteroscope is passed over the second guide wire up to the level of interest; then the working wire is removed and the safety wire is left in place. The placement of these wires must be done with great care, because problems arising from these initial steps may cause difficulty

later in the case (perforation, injury to ureteral orifice). The use of a safety wire during these procedures is essential to maintain access and to avoid turning a minor complication into a major one.

Complications

Over the past decade, the instrumentation in ureteroscopy has improved. Large rigid endoscopes of 11F or more in size have given way to semirigid endoscopes of 6–8F size, and 7F flexible ureteropyeloscopy with large working channels, up to 3.6F. Subsequently, the complication rates have improved significantly. Table 53.1 gives the complication rates in the early ureteroscopy era (pre-1992) and more recent studies (post-1992).

Pain and colic

The true incidence of pain and colic is difficult to discern because few prospective studies have been employed to look at this subjective parameter and also the presence of ureteral stents after ureteropyeloscopy may cause discomfort unrelated to the actual procedure. Early series report colic rates of 9–25%, although the higher number represents questionnaire data that would naturally increase this figure.<sup>4,5</sup> Modern series show the incidence between 3 and 5%.<sup>6,10,11</sup> The etiology of pain may be ureteral obstruction caused by edema of the ureteral wall, retained stone fragments, or

Table 53.1 Complications of ureteroscopy: comparison of early and modern series

| Study                    | Year | No. | Indication<br>for procedure                    | Colic<br>pain | Minor comp<br>Lic<br>ation | Major complication |                      |                    |                            |  |       |                        |                 |               |              |             |   |
|--------------------------|------|-----|--|---------------|----------------------------|--------------------|----------------------|--------------------|----------------------------|--|-------|------------------------|-----------------|---------------|--------------|-------------|---|
|                          |      |     |  |               |                            | Fever              | False<br>pass<br>age | Mi<br>nor<br>bleed | Pro<br>Lon<br>ged<br>bleed | Extra<br>Vas<br>ation<br>or minor<br>perforation | UTI   | Pyelo<br>Nep<br>hritis | Perfo<br>ration | Stri<br>cture | Av<br>ulsion | Uri<br>noma | Uro<br>sepsis                                 |
| Pre-1992                 |      |     |  |               |                            |                    |                      |                    |                            |  |       |                        |                 |               |              |             |   |
| Carter <sup>1</sup>      | 1986 | 125 |  | 5.60%         | 17.60%                     |                    |                      |                    |                            |  | 1.60% | 4%                     | 4%              |               |              | 1%          |   |
| Schultz <sup>2</sup>     | 1986 | 100 |  |               |                            |                    |                      |                    |                            |  | 4     | 4                      | 1               |               |              |             |   |
| Blane <sup>3</sup>       | 1988 | 346 |  |               |                            | 6.20%              | 0.90%                | 0.50%              | 0.30%                      | 0.60%  |       | 4.60%                  | 1.40%           | 0.60%         | 0.60%        | 0.30%       |   |
| Stoller <sup>4</sup>     | 1992 | 156 |  | 25%           | 12%                        |                    |                      | 2%                 |                            |  |       | 15%                    | 3.60%           |               |              | 1.90%       |   |
| AbdelRazzak <sup>5</sup> | 1992 | 290 |  | 9%            |                            | 6.90%              |                      | 2.10%              | 1%                         | 1%   | 1%    | 1.70%                  | 0.70%           |               |              | 5.20%       |   |
| Post -1992               |      |     |  |               |                            |                    |                      |                    |                            |  |       |                        |                 |               |              |             |   |
| Grasso <sup>6</sup>      | 1998 | 584 | 52% stone tumor, 17% endopyelotomy             | 5.50%         |                            | 1.40%              |                      | 0.70%              | 0.20%                      |  | 1.60% | 0.50%                  | 0.00%           | 0.50%         | 0.00%        | 0.00%       | CVA 0.2% DVT 0.2%                             |
| Grasso <sup>7</sup>      | 1998 | 66  | 100% stone > 2 cm                              |               |                            |                    |                      |                    |                            |  | 1%    |                        |                 |               |              |             | CVA 2%, clot retention 2%                     |
| Mugiy <sup>8</sup>       | 2000 | 104 | 100% impacted                                  | 00            |                            |                    |                      |                    | 00000                      |  | 000   | 0                      |                 |               |              | 0000        | 0   |
| Devaranjan <sup>9</sup>  | 1998 | 300 | 100% laser lithotripsy                         |               |                            | 2.00%              |                      |                    |                            |  |       | 4%                     | 3%              | 0             |              | 0.30%       | 6% Peritonitis 0.3%, perinephric abscess 0.3% |
| Hendrikx <sup>10</sup>   | 1999 | 87  | 100% mid and distal ureter                     | 3.40%         | 3.40%                      | 3.40%              | 0.00%                | 0                  | 2.3                        | 10.30%   | 2.30% |                        |                 |               | 1.10%        | 1.10%       |   |
| Hammon <sup>11</sup>     | 1997 | 209 | 67% stone 28% diagnosis, 5% stent manipulation | 3.50%         |                            | 2%                 |                      | 0                  | 0                          |  |       | 1%                     | 0.50%           |               | 000          | 2.50%       | CVA 0.5%                                      |

CVA, cerebrovascular accident; DVT, deep vein thrombosis; UTI, urinary tract infection.

extravasation into the retroperitoneum. Pain should be treated with analgesics, which may include opiates as well as nonsteroidal anti-inflammatory agents. Urinary drainage via ureteral stent or percutaneous nephrostomy may be needed to relieve pain that does not respond to analgesics.

### ***Postoperative pain and stenting***

The standard teaching had been to leave a ureteral stent after all ureteroscopic procedures. It was believed the stent decreased postoperative obstruction due to retained stone fragments and ureteral edema, in addition to preventing ureteral stricture formation. Recent prospective studies have assailed this concept, indicating that a great deal of postoperative discomfort is related to the stent itself and not to the procedure.<sup>12–14</sup> Hosking et al noted that 43% of his unstented patients had no pain, and 48% had mild postoperative pain after ureteroscopy.<sup>14</sup> Two randomized controlled studies between stented and unstented patients showed decreased flank pain and bladder discomfort in the unstented groups compared with stented groups, although in one study all 4 patients that needed postoperative hospitalization were members of the unstented group.<sup>12,13</sup> No strictures developed in any of the unstented groups in these three studies. The current recommendation is that stents are reserved for patients with ureteral damage or edema from long-standing impactions and for difficult procedures in which ureteral trauma is encountered.

### **Infectious complications**

Because of the retrospective nonstandard nature of reporting of complications, it is difficult to discern whether fever is caused by infection or related to retroperitoneal inflammation. It is also difficult to differentiate urinary tract infection from pyelonephritis in the stented patient where the stent provides a direct conduit to the upper urinary tract. The incidence of infectious complications has decreased in the modern era and can be estimated at 1–2%.<sup>1–11</sup> Urosepsis is rarely reported and has an incidence of less than 1%.<sup>1–11</sup> Aggressive treatment should be dictated by the patient's clinical status, with hospitalization and intravenous antibiotics reserved for patients with urinary infection associated with high fever or signs of sepsis. The role of prevention in the form of negative preoperative urinary cultures and prophylactic antibiotics cannot be overemphasized.

### **Failure to access/failure to visualize**

Earlier studies with large-caliber, rigid ureteroscopes found rates of inability to access the ureter or advance the telescope to the stone at up to 12%.<sup>4</sup> Modern small-caliber instruments, judicious use of balloon dilation, and hydrophilic guide wires for bypassing difficult portions of the ureter have made this complication very rare. When it is not possible to access the ureter because of false passage at the ureteral orifice or perforation, it is advisable to place a ureteral stent over the safety guide wire and return 1–2 weeks later. If no access to the ureter is available, selected patients may require percutaneous nephrostomy.

### **Bleeding**

Serious bleeding is very uncommon; however, even moderate bleeding can disrupt visualization and may result in incomplete stone fragmentation or tumor resection. Incidence rates in modern series indicate that this occurs in 1–10% of cases, rarely with

prolonged or serious bleeding requiring transfusion.<sup>6–11</sup> Although severe bleeding after antegrade endopyelotomy or retrograde balloon catheter endopyelotomy is not uncommon, the incidence with ureteroscopic incision has been low, 0–2.5%, with the majority of series reporting no serious postoperative bleeding.<sup>15–19</sup> Treatment of bleeding intraoperatively to improve vision may include direct cauterization, pump irrigation, and use of a ureteral sheath to assure good outflow. Severe bleeding needs to be treated supportively with fluid resuscitation and blood transfusions. Severe, persistent bleeding that does not resolve may require selective angiographic evaluation and treatment.

### **Perforation/false passage/ extravasation**

Perforation may be graded as minor, such as with a guide wire (<1 mm), or major, such as with a ureteroscope or dilator. The incidence of this complication, especially major perforations, has decreased according to recent studies, and is reported at 0–10%.<sup>6–12</sup> Risk of perforation will increase with impacted stones and may be prevented with use of hydrophilic guide wire and stiff open-ended ureteral stent to bypass the obstructing stone. Schuster et al noted that perforation rate was associated with increased operative time, decreased surgeon experience and presence of stone in the kidney.<sup>20</sup>

Minor perforations, such as those caused by guide wires, do not necessitate termination of the procedure. If the perforation is easily bypassed, the procedure may be completed, although it is advisable to use a stent at the end of the operation. These perforations generally will heal without sequelae. Major perforations, requiring immediate operative repair or urinary diversion, were reported as 4–15% in earlier studies. However, this complication is rare in contemporary series.<sup>1–12,20</sup> Severe perforations have also been reported to cause peritonitis.<sup>9</sup> Use of a safety guide wire is essential to ensure urinary tract continuity and avoid operative intervention.

Perforation resulting in stone extrusion outside of the ureteral lumen has been the subject of several reports. Grasso et al used endoluminal ultrasound to conclude that the severity of complications is based on the number of fragments and their location in the ureteral wall. Single small fragments less than 2 mm deep should be removed to prevent obstruction and stricture formation. Fragments more than 4 mm deep do not cause obstruction and do not need treatment. The most problematic patients are those with multiple small submucosal fragments within 4 mm of the surface,<sup>21</sup> and they need to be monitored closely for development of obstruction. Stones in the intramural ureter have been shown to cause granuloma formation and obstruction, which is amenable to endoscopic management.<sup>22</sup> Several other retrospective studies have shown the incidence of paraureteral stone extrusion to be about 1%.<sup>23–25</sup> The extrusions are usually associated with lithotripsy and stone manipulation that includes pushback of the ureteral stone to the renal pelvis, procedures which have generally been abandoned in the modern era. The extrusions are more likely to occur in the ureter above the iliac vessels. The retroperitoneal stones cause no infectious complications and can safely be left in place, although they may prove bothersome on future plain radiographic studies and require a subsequent intravenous pyelogram to rule out a calcification within the urinary tract.

### Stricture

Stricture is one of the serious long-term concerns after ureteroscopy (Figure 53.1). The use of smaller ureteroscopes, with decreased need for dilation for scope access, and the widespread adoption of improved techniques have decreased the rate of this complication from 0.7–3.6% in



**Figure 53.1** Retrograde pyelogram demonstrating middle ureteral stricture.

earlier studies to less than 1% in recent reports.<sup>1–12</sup> The etiology of this complication is multifactorial and may be related to the ureteral reaction to long-standing stone impaction, ureteral trauma from scope or dilator introduction, injury from the lithotripsy device, especially electrohydraulic lithotripsy (EHL), electrocoagulation injury (during tumor resection), or to the presence of foreign bodies in the ureteral wall. Roberts et al analyzed 21 patients with successful treatment of stones impacted for more than 2 months



and found that ureteral strictures developed in 5 patients (24%) at the site of stone impaction during a mean follow-up period of 7 months. In 4 of the 5 patients, perforation at the stone site occurred during a previous unsuccessful attempt at stone removal.<sup>26</sup> Other studies, albeit with shorter follow-up, have not shown a relationship between stone impaction and subsequent stricture formation, emphasizing the role of the previous perforation on stricture formation.<sup>8</sup>

Because of the decreasing incidence of strictures, recent focus has been placed on the decreased need for follow-up radiographic studies to detect postureteroscopic strictures. Earlier practice made use of postureteroscopic imaging with either excretory urography, sonography, or noncontrast helical computer tomography (CT) mandatory. Two retrospective analyses showed that in patients without preoperative obstruction or postoperative pain, the incidence of stricture or residual significant fragments is zero.<sup>27,28</sup> Another report retrospectively reviewed 241 procedures and found an incidence of postureteroscopy obstruction of 12%. Of that group, 7 patients had no symptoms, thus yielding a 2.7% rate of silent obstruction. Unlike previous studies, this study found that preoperative obstruction did not correlate with postoperative obstruction.<sup>29</sup> Until a definitive prospective study is completed, it is prudent to recommend postoperative imaging studies on all ureteroscopy patients 6–12 weeks after the procedure.

### **Avulsion**

Ureteral avulsion is a devastating injury usually resulting from a vigorous attempt to remove a large stone or fragment with a basket, often above the iliac vessels. This complication is increasingly rare in modern series, but still occurs, with an incidence much less than 1%.<sup>6–11</sup> These injuries can be avoided by minimizing the use of a basket extractor above the iliac vessels, and instead relying on a lithotripter (laser, EHL) to completely fragment the calculus. If an extractor is used, consider the three-pronged grasper, or one of several newly introduced grasping devices that allows easy release of stone fragments. If a basket does become entrapped in the ureter, do not use force to remove it. Instead, disarticulate the basket and remove the ureteroscope. Reintroduce the ureteroscope and lithotripsy the stone retained within the basket. Care must be taken not to cut the wire(s) of the basket with a laser lithotripsy. After fragmenting the stone to less than 2 mm, the retained basket is simply removed. If this should fail, arrange for drainage of the affected renal unit and a secondary procedure to remove the device or to fragment the stone—percutaneous nephrolithotomy or extracorporeal shock wave lithotripsy (ESWL). Most avulsions result in long segments of non-functioning ureter. If the avulsion is below the iliac vessels, a ureteral reimplant should be attempted. If it is above the iliac vessels, an ileal ureteral or, substitution, renal autotransplantation should be considered, or even a nephrectomy if function is poor in the affected kidney.<sup>30</sup>

### **Urinoma/perinephric abscess**

These rare complications occur much less than 1% of the time. Their etiology may be related to high intraoperative pressures in the collecting system due to forceful irrigation with limited drainage. They may also result from poor postoperative drainage in an

obstructed system. These conditions usually respond well to percutaneous drainage and appropriate antibiotic treatment.

### General medical complications

Patients may suffer the same variety of perioperative insults as those associated with any other surgical procedure. Several reports have cited cerebrovascular accidents (CVAs) during ureteroscopy, but no firm association has been proven.<sup>6,7,11</sup> One should maintain a high index of suspicion for deep vein thrombosis (DVT) and pulmonary embolism in patients with known risk factors, especially those in stirrups during prolonged procedures. Prophylaxis with intermittent venous compression devices should be standard procedure.

**Vesicoureteral reflux.** Vesicoureteral reflux after ureteroscopy has been reported in 2.7–10% of patients undergoing ureteroscopy.<sup>4,31</sup> Richter et al found that the condition was temporary and resulted in no long-term sequelae.<sup>30</sup> One case report did note a stone developing in the dilated intravesical ureter after ureteroscopy.<sup>32</sup>

**Foreign body.** Foreign bodies may rarely be left in the urinary tract, and include ‘forgotten’ ureteral stents, stone retrieval baskets, laser fibers, and guide wires.<sup>33–36</sup> The laser lithotripter has greatly improved capabilities for fragmenting urinary stones in a variety of locations. Unfortunately, this device may also fragment guide wires and stone baskets with equal efficiency. Care must be taken to avoid damage to these instruments while using the laser. In addition, two case reports have documented retained laser fibers as a source of potential ureteral obstruction or calculus formation.<sup>33,34</sup> The endoscopist must be careful when using laser devices and mindful of potential consequences of a retained foreign body. Most small foreign bodies are amenable to endourologic removal.

### Percutaneous renal surgery

Technological advances have brought percutaneous renal surgery into the armamentarium of the general urologist. Percutaneous renal surgery is now indicated for calculus removal, endoscopic pyelotomy, and management of upper tract transitional cell cancer. It is incumbent on practicing surgeons to be knowledgeable about the complications associated with percutaneous renal surgery in order to avoid common errors and ensure a successful outcome for their patients.

The procedure most commonly performed via the percutaneous route is calculus removal. Generally, renal stones larger than 2 cm, staghorn calculi, and large ureteral stones not amenable to ureteroscopy are approached percutaneously. In addition, patients undergoing endopyelotomy, especially those with significant stone burden, are candidates for percutaneous renal surgery. Patients with upper tract transitional cell carcinoma in the kidney or upper ureter may also be approached percutaneously, if the lesions are not amenable to ureteroscopic ablation. Percutaneous renal surgery is now associated with success rates as high as 80–90%.<sup>37</sup> The procedures are minimally invasive and often require short hospital stays, generally of 1–2 days. Modern techniques and equipment have helped lessen complication rates.

*Preoperative*

Preoperatively, the patient must be evaluated with a detailed history and physical examination to eliminate or improve risk factors for surgery. Absolute contraindications for percutaneous renal surgery include uncorrected bleeding diathesis, active urinary tract infection, and general medical conditions that preclude the safe administration of anesthesia in the prone position. Relative contraindications may include body habitus (severe obesity) and orthopedic conditions that may make positioning difficult.

Laboratory examinations should include complete blood count, urinalysis and urine culture, and pregnancy test for women. A chest radiograph, electrocardiogram, and internal medicine consult are ordered when appropriate. Blood should be sent for a type and screen in case transfusion is needed. The value of coagulation studies, such as prothrombin time (PT) and partial thromboplastin time (PTT), is questionable in patients with no history of bleeding diathesis.<sup>38,39</sup> Preoperative imaging of the urinary tract should include a kidney, ureter and bladder (KUB) radiograph, as well as either an excretory urogram or thin-cut helical CT of the abdomen and pelvis for stone localization and definition of the anatomy. Renal ultrasound may be obtained when appropriate, but is less helpful in surgical planning. If suspicion of poor renal function is entertained, a preoperative renal scan may be obtained to determine renal function.

DVT, which may lead to pulmonary embolism, is always a concern with these procedures.<sup>40</sup> Use of pneumatic compression devices in the lower extremities is essential to prevent this potentially devastating complication.

*Operative factors***Positioning**

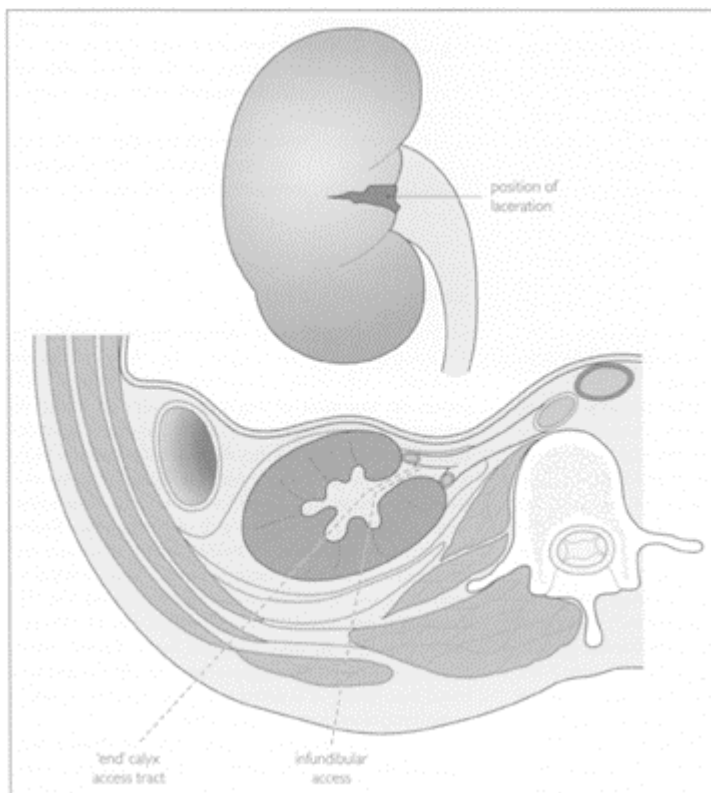
Although percutaneous renal surgery has been successfully performed with the patient in the lateral and supine positions, the most common patient position is prone. This requires that the anesthesia team be thoroughly familiar with this position and have supplies and padding to support the head and maintain an adequate airway. Percutaneous renal surgery may be performed using local, spinal, or general anesthetics, although most extensive surgery will require general anesthesia to prevent patient movement during delicate surgical maneuvers. Adequate padding of the prone patient should include 'chest rolls', placed along the lateral edges of the patient's abdomen and thorax, which should run from the clavicle to the iliac crest. These pads should be adjusted for patient size and must raise the abdomen off the table to allow for adequate diaphragmatic excursion and ventilation. In addition, care must be used when positioning the arms. The arms may be tucked by the patient's side or placed above his head. The above-the-head position gives the anesthesia team access to the upper extremities during the procedure, but care must be used to keep the arm abducted below 90°. The forearms should be supported with well-padded arm boards, and 'axillary rolls' should be placed to support the brachial plexus and prevent undue tension on this nerve bundle. The lower extremities must be padded with care to protect the bony prominences of the knees and toes. A small wedge-shaped pillow placed beneath the ankle is useful for keeping the knees slightly flexed.

### Percutaneous access

The proper location of the percutaneous puncture into the kidney is the key to a successful outcome. The access may be obtained by the radiologist or the urologist. If placed by the interventional radiologist, it is essential that the urologist participate in the planning and be available during the access placement. A thorough understanding of the anatomy of the kidney and its relation to surrounding structures will allow safe, successful placement of the access catheter.

The key for all percutaneous punctures is to achieve access directly into the calyx via a puncture that is directed end-on to the renal papilla (Figure 53.2). In an extensive set of studies involving cadaveric kidneys, Sampaio and his associates have detailed the vascular relationships to the intrarenal collecting system.<sup>41-43</sup> In a study using 62 cadavers, retrograde pyelograms and corresponding three-dimensional resin casts were made of the collecting system, arteries, and veins of fresh cadavers,<sup>41-42</sup> looking for the effect of percutaneous punctures into various sites in the kidney. In these studies, access directly into the infundibulum was compared with access into the calyx. Upper pole access into the infundibulum resulted in 67% vascular injuries, with 26% being arterial injuries. The most common serious injury was to the posterior segmental artery. This vessel crossed the posterior surface of the upper infundibulum in 57% of cases.<sup>41,42</sup> This artery may supply as much as 50% of the renal parenchyma.<sup>42</sup> Middle pole access via an infundibulum yielded a 23% arterial injury rate, with the middle branch of the posterior segmental artery most commonly affected. Inferior pole infundibular punctures had an arterial injury rate of 13%, with 38% of the kidneys having a significant artery located posterior to the collecting system. When end-on calyceal access was obtained, only 8% of kidneys showed a vascular injury: only veins were injured; no arteries were affected. This low injury rate for end-on punctures was unrelated to upper, middle, or lower pole location of the accessed calyx.<sup>41,42</sup>

Upper pole renal access carries the additional risk of injuries to the pleura and lung. Pneumothorax and hydro thorax are the most common injuries (6%); lung parenchymal injury is rare.<sup>44,45</sup> The diaphragm is traversed by all intercostal punctures and even some punctures below the 12th rib.<sup>46-48</sup> The pleura often extends caudally



**Figure 53.2** Safe percutaneous renal access is directed through an end calyx into the collecting system. Potential risk of segmental artery injury increases with infundibular access. (Reproduced with permission from Fuchs et al.<sup>37</sup>)

to the 12th rib; the lower edge of the lung usually remains above the 11th rib. Regardless of the stage of respiration, risk of injury to the lung makes a 10th intercostal space approach prohibitive.<sup>46,49</sup> A puncture above the 12th rib is associated with a 6–32% incidence of hydrothorax (mean 15%). Despite this relatively high occurrence, the injuries required drainage in only 5% of cases.<sup>49</sup> Pleural injuries may be recognized by ventilatory difficulty or fluoroscopy at end of procedure. Postoperatively, the patient may experience chest pain and dyspnea. Treatment should consist of aspiration of the pneumohydrothorax or chest tube placement. As with all complications, prevention is the goal. Limiting upper pole access below the 11th rib and use of preoperative prone CT may help. Fuchs et al noted that the use of prone spiral CT may help prevent

complications: they experienced only 3 cases of pleural irritation in 75 cases, with no direct pleural injury.<sup>37</sup> In contrast, two other large series of supracostal cases showed a 7–9% incidence of thoracic complications.<sup>50,51</sup> Because of the increased risk of complications, the supracostal access should be approached cautiously and only when complex renal anatomy or stone burden warrants its use.

Even in punctures that remain below the ribs, injuries to nearby structures are possible. Certain predisposing conditions, such as alcoholism (possible hepato-splenomegaly), should be identified preoperatively. The risks of splenic or hepatic injury increase in mid or full inspiration and with hepato- or splenomegaly.<sup>46</sup> Injuries may be prevented through lower pole access and use of preoperative prone spiral CT or real-time ultrasound during puncture. If hepatic injury is recognized postoperatively, consideration should be given to placing a ureteral stent and catheter to provide drainage of the bladder and to prevent renobiliary fistula.<sup>37</sup> Injuries to the spleen are rare.<sup>52</sup> Splenic injury will cause significant bleeding and may be recognized by hypotension in the absence of a bloody procedure. The diagnosis is made intraoperatively or postoperatively with a CT. Treatment should be splenectomy.

The large and small bowel are other potential sites of injury during percutaneous renal access. Occasionally, the retroperitoneal colon may lie in a posterolateral or retrorenal position.<sup>53–55</sup> In these cases, the retroperitoneal colon is most likely situated near the inferior pole of the kidneys. This condition has a frequency of 1.9% when the patient is in the supine position but 10% when in the prone position. The presence of horseshoe kidneys is associated with increased risk of retrorenal colon, and thus awareness should be heightened when horseshoe kidney is present.<sup>56</sup> Fuchs et al noted that risk factors include left renal disease, chronic constipation, abdominal surgery, and mobile kidneys. If the patient is at high risk, a preoperative abdominal CT with the patient in a prone position and intraoperative real-time ultrasound during the puncture should be considered.<sup>37</sup>

Gerspach et al reported a series of 5 bowel injuries over a 5-year period in a multicenter study. All of the injuries were extraperitoneal. They concluded that young lean males with minimal retroperitoneal fat were more likely than other patients to have a retroperitoneal colon, and thus were more susceptible to bowel injuries. It was suggested that access in high-risk patients be obtained more medially and superiorly than normal. Four of the 5 injuries were observed postoperatively. The presenting features included fever, fecaluria, abdominal pain, and leukocytosis. All of the patients were treated with conservative management. If colon perforation is discovered intraoperatively, removal of the nephrostomy tube from the kidney with placement of a drain in the bowel should be attempted. If successful, then replacement of the nephrostomy tube access more superiorly and medially should be performed to complete the nephrolithotomy. At the conclusion of the procedure, the kidney may be drained via nephrostomy tube or via double-J ureteral stent and Foley catheter. The drain in the bowel is replaced with a pericolic Penrose drain. If injury is discovered postoperatively, the nephrostomy tube is withdrawn from the kidney to the bowel, a double-J ureteral stent and Foley catheter are placed, and the patient is given intravenous antibiotics, bowel rest, and parenteral nutrition. The tube is gradually withdrawn from the bowel (Figures 53.3 and 53.4). Intraperitoneal injuries to the bowel, although extremely rare, should be treated with open surgical repair.<sup>57</sup>

The duodenum, which lies anteromedial to the right kidney, has been the rare site of injury. If this structure is injured, gastric rest, nasogastric tube, and observation may be used.<sup>37,58,59</sup>

### **Vascular/bleeding**

Severe bleeding is the most common serious complication of percutaneous renal surgery. An AUA (American Urological Association) consensus panel reviewed 110 papers on treatment of staghorn calculi and found the average transfusion rate was 10.8%.<sup>60</sup> The use of a balloon catheter for tract creation may decrease intraoperative blood loss below that created with Amplatz dilators.<sup>61</sup> Stoller et al found that the average blood loss from an uncomplicated, single-puncture PNL was 2.8 g/dl of hemoglobin. Factors that increased blood loss included multiple punctures and renal pelvic perforation, whereas use of a mature nephrostomy tract was associated with decreased blood loss. The transfusion rate was 23% overall, with a rate of 14% in a single puncture in uncomplicated cases. Factors which affected transfusion included preoperative anemia and total blood loss. Stoller et al noted that their transfusion rate in recent procedures was lowered to 4%.<sup>62</sup>

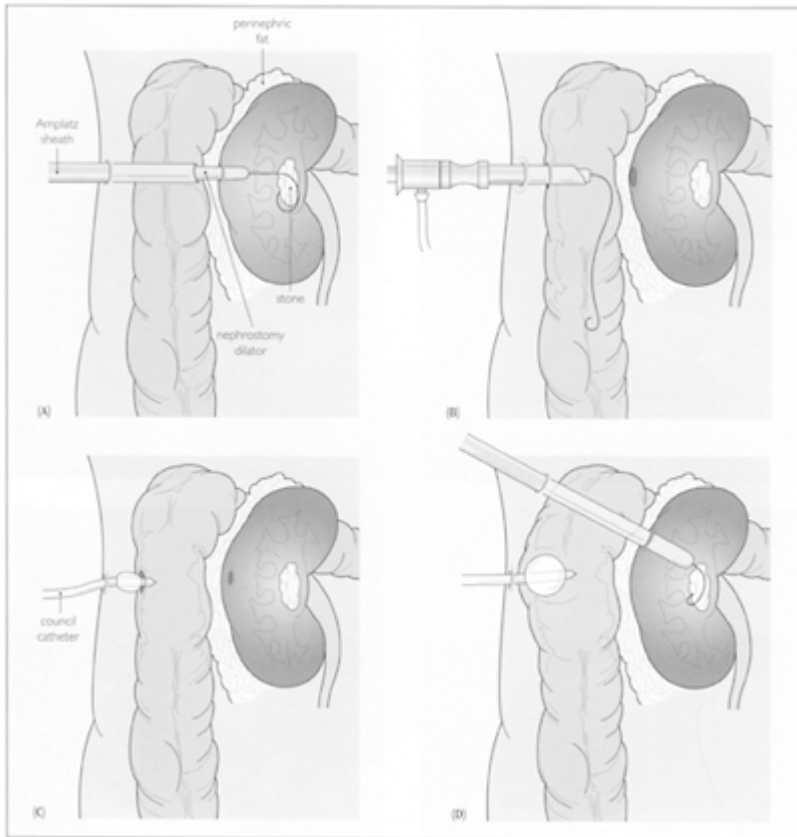
Postoperative bleeding should first be treated with conservative, supportive measures. Direct pressure using a slightly inflated Foley catheter or Kaye nephrostomy



**Figure 53.3** Percutaneous access injury to colon. (A) Intravenous pyelogram, demonstrating a large renal pelvic stone. (B) Intraoperative middle and lower pole calyx percutaneous access is obtained for stone extraction. (C and D) Status post percutaneous nephrolithotomy pneumogram and contrast injection through lower nephrostomy tube delineates injury to sigmoid colon. (Courtesy of Dr



Weiner, The Methodist Hospital,  
Houston, Texas.)



**Figure 53.4** Treatment of percutaneous injury to colon. (A) The nephrostomy sheath is in place. (B) After nephroscopic insertion, the sheath and safety wire is pulled back into the colon. The guide wire is advanced into the colon. (C) A 22F council-tip catheter is placed into the colon coaxially over the guide wire. (D) Secondary percutaneous access is obtained through an upper pole calyx site that is superior and medial to the

original percutaneous access site.  
(Reproduced with permission from  
Gerspach et al.<sup>57</sup>)

balloon should be attempted. If brisk bleeding is noted in the nephrostomy tube, the tube should be clamped. Mannitol has been suggested to decrease bleeding by swelling the kidney and forcing a diuresis. The efficacy of mannitol in this situation has not been subjected to formal trials. Kessaris et al reviewed 2200 percutaneous renal procedures and found a 0.8% rate of serious hemorrhage requiring angiography and selective embolization. They found 7 patients had an arteriovenous fistula (AVF), 4 had a pseudoaneurysm, 2 had an AVF and pseudoaneurysm and 2 had a lacerated renal vessel. They found that 24% of these complications occurred in the immediate postoperative period after a trial of clamping the nephrostomy and balloon tamponade, 41% occurred in the period from 2–7 days postoperatively, when 3–4 units of blood transfusions were given after the immediate post-operative period, and 35% of patients had sudden hemorrhage more than 7 days after the percutaneous renal surgery. After the embolization procedure, 15 required no further treatment, and 2 patients required an open operation. They could identify no preoperative risk factors for bleeding.<sup>63</sup>

Martin et al showed a similar 1% rate of serious postoperative bleeding in 808 patients over a 14-year period. AVF and pseudoaneurysms were most commonly diagnosed. All patients were treated with hyperselective embolization (Figure 53.5). This was effective in 7/8 patients; one required partial nephrectomy.<sup>64</sup>

### **Vascular complications of endopyelotomy**

Sampaio studied the vascular relationships for endopyelotomy. In 65% of kidneys, a prominent artery or vein was noted in close relationship with the anterior ureteropelvic junction (UPJ). The most commonly affected artery was the inferior segmental artery. In 6.2% of cases, a large vessel was found directly related to the posterior surface of the UPJ. The incidence of significant hemorrhage with posterolateral incision is 12%.<sup>48</sup> With posterior or posterolateral incision an injury may occur to the posterior segmental artery which may supply up to 50% of the parenchyma. Although controversy exists regarding the proper way to make the incision in endopyelotomy, and various imaging modalities—from MR (magnetic resonance) and CT angiography to endoluminal ultrasound have been advocated, the direct lateral incision will avoid all important vessels.<sup>65,66</sup>

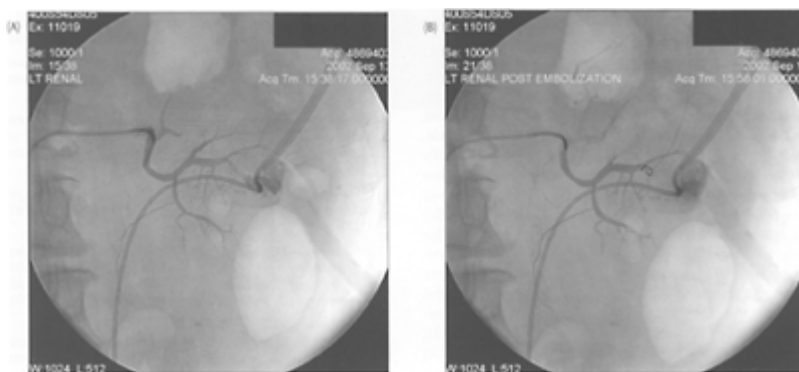
### **Fluid absorption**

Fluid absorption may occur from PNL, especially when a closed sheath system is used. A recent study found that fluid absorption during PNL is estimated to be between 44 ml and 474 ml. This varies with the amount of irrigant used and the duration of the procedure. Absorption decreases with use of a low-pressure Amplatz sheath and staged procedures (access and PNL done on separate occasions). Absorption increases with significant perforation and bleeding. No patients demonstrated clinical or biochemical evidence of

electrolyte imbalance.<sup>67</sup> Of note, another study showed that patients with extravasation and extrarenal fluid absorption had more pain and slower postoperative recovery than did patients with intravascular fluid absorption.<sup>68</sup> In general, use of open sheath systems with normal saline irrigation should result in few complications when there is minimal perforation of the collecting system.

### Infectious complications

Fever is a common postoperative finding that occurs in 23–42% of cases.<sup>69–71</sup> The cause may be extravasation of



**Figure 53.5** (A) Selective segmental renal arteriogram demonstrating significant bleeding from a middle (distal) segmental renal artery injured during percutaneous access. (B) Successful selective segmental embolization of middle renal artery bleeding site. (Courtesy of Dr Weiner, The Methodist Hospital, Houston, Texas.)

fluid into the retroperitoneum or intravascular absorption of bacteria from the urinary tract. One study of postoperative patients with negative preoperative urine cultures and prophylactic antibiotics demonstrated no significant sequelae from the fevers.<sup>70</sup> Although intrarenal pressures may reach 30 mmHg in up to 26% of patients during percutaneous renal surgery, increased pressures were not found to correlate with postoperative fevers.<sup>71</sup> Correlation of fever with infectious vs noninfectious stone type has not been consistent between studies.<sup>70,71</sup> Guidelines to prevent postoperative infection include negative preoperative urine cultures, prophylactic antibiotics, and use of lowpressure irrigation

with an open-access sheath and maintenance of the irrigating fluid pressure below 30 cmH<sub>2</sub>O.

### **Hypothermia**

Hypothermia has several consequences in the postoperative patient, including coagulopathy, increased metabolic requirements, and prolonged recovery from anesthesia. Because of large areas of exposed body surface, long operative times, and use of room temperature irrigant, patients undergoing percutaneous renal surgery are at risk of developing significant hypothermia. Core temperatures have been noted to fall almost 2°C on average during PNL.<sup>72</sup> The use of warmed irrigation fluids has not been shown to improve this finding consistently, although more profound temperature drops were found in patients with room temperature irrigant.<sup>73</sup> Use of appropriate blankets and bear hugger devices as well as warmed irrigant are simple preventive measures for hypothermia.

### **Transitional cell carcinoma**

Percutaneous renal surgery has been used to manage transitional cell carcinoma of the kidney in a minimally invasive fashion. Patients who are poor operative risks, those with solitary kidneys, and those with certain low-grade, localized tumors may be managed either ureteroscopically or percutaneously. While percutaneous management has been suggested for a variety of tumors, it is better reserved for patients with large tumor burden. Those with smaller tumor burden may be managed via the ureteroscope. This has the advantage of not exposing tissues in the nephrostomy tract to transitional cell carcinoma. Although some investigators have not noted any problems,<sup>74</sup> several reports have demonstrated tumor seeding of the nephrostomy tract.<sup>75,76</sup> Recurrence rates for low-grade (grade 1–2), low-stage tumors in patients treated with adjuvant BCG (bacille Calmette-Guérin) therapy are acceptably low (25%). Renal-sparing endoscopic management may be an appropriate choice for patients who are compliant with a strict follow-up regimen.<sup>77</sup>

### **Conclusions**

The past 25 years have witnessed a revolution in surgery from open procedures to minimally invasive management with endoscopy. These less-invasive procedures have come at a cost, including large learning curves for practitioners, and the recognition of a new set of morbidities specific to endourologic surgery. Thorough familiarization with the diagnosis and management of these complications has led to greater acceptance of minimally invasive management in the general urologic community.

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## Complications of urological laparoscopy

Sam B Bhayani and Louis R Kavoussi

### Introduction

Over the past decade, urologic laparoscopy has evolved from an experimental technique to an efficacious and popular surgical modality. As the field has matured, investigators have recognized the complications of performing urologic laparoscopy. Although many complications are an inevitable part of practice, risks can be decreased by the informed laparoscopist. The surgeon who offers minimally invasive surgery must be prepared to manage or avoid these complications when subjecting patients to laparoscopic procedures. Overall, the complication rate of urologic laparoscopic procedures is 3.5–11.9%. Reoperation is required in 0.08–1.1% of cases, and the mortality rate is approximately 0.09%.<sup>1–5</sup> Although these results have largely been published by experienced laparoscopists, they demonstrate that the knowledgeable surgeon can safely offer laparoscopic alternatives to major open surgeries. As with open surgery, complications are more prevalent in complex procedures and are more common earlier in the learning curve. Hence, initial cases should be highly selected, and open instruments should be readily available. As the surgeon's comfort level and experience grow, more complex procedures can be attempted.

To recognize, manage, and ultimately minimize complications, the laparoscopist must be familiar with laparoscopic physiology and laparoscopic surgical anatomy. Additionally, the surgeon must have an intimate knowledge of the complex equipment used in performing the operations. Also, given the limited operative view, the surgeon must strive to understand not only what is in the operative field but also what is in the nonvisualized visceral structures. Finally, when discussing risks of laparoscopic surgery, the patient should be informed of the possibility of open conversion in all cases.

Complications may arise at any point in the procedure, from positioning of the patient to postoperative management. The operating room (OR) team must be vigilant in recognizing potential problems at any time during the case. Effective communication between the surgeon, assistants, anesthesiologist, and staff is desirable. All OR personnel should be familiar with laparoscopic and open surgical equipment and monitors.

### Complications from positioning

Laparoscopic procedures are sometimes longer than their open counterparts. Also, extremes in table movement may be needed so that the bowel can be moved out of the operative field. Consequently, proper padding of the patient's pressure points is necessary. Neuromuscular injuries are infrequent, but may contribute to patient morbidity. A recent multi-institutional study of 1651 patients undergoing urologic laparoscopic procedures revealed a 2.7% incidence of neuromuscular injury.<sup>6</sup> Injuries



were more common with upper retroperitoneal procedures (3.1%) than with pelvic laparoscopy (1.5%). Patients in the full flank position were found to be more prone to neuromuscular injury than those in the partial flank position. Rhabdomyolysis occurred in 6 patients (0.4%); all had undergone upper retroperitoneal laparoscopy, were heavier, and underwent longer procedures. Institutions with higher volumes of laparoscopic procedures had a lower incidence of complications.

Neuromuscular injuries can be minimized by close attention to padding and positioning of the patient. Heavier patients undergoing retroperitoneal procedures should be informed of their increased risk of these injuries. Hidden pressure points, such as the axilla, legs, and arms, should be carefully checked after all manipulations of the OR table. Patients with little body fat are at risk for rhabdomyolysis. Therefore, hard surfaces such as a beanbag should be avoided. Rhabdomyolysis should be considered in patients with low urine output, extensive muscle pain, or darkened urine. A serum creatine kinase level will be elevated, and urine myoglobin may be increased. Treatment is largely supportive; volume expansion and urinary alkalization are recommended, and diuretics can be used to maintain urine output. Acute renal failure may require consultation with a nephrologist and temporary dialysis. In the majority of cases, renal function will improve.

Neuromuscular problems may also affect the surgeon. After performing laparoscopic procedures, urologists reported pain in their necks, shoulders, backs, wrists, and hands at frequencies of 17–67%.<sup>6</sup> Some surgeons required professional consultation for their injuries. To minimize these injuries, the surgeon must be positioned for comfort and efficiency. Monitors must all be within the surgeon's sight, and pedals for dissecting instruments should be placed in an ergonomic fashion. The table height must be adjusted to the surgeon's comfort level to minimize fatigue. Standing stools are commonly used. Additionally, various laparoscopic OR environments have been engineered to enhance surgeon comfort and control (OR1, Karl Storz, Tuttlingen, Germany; Hermes, Stryker: Endoscopy, San Jose, California). These systems include highly mobile video monitors and voice or touchscreen control of lighting and insufflation.

### **Complications with access and insufflation**

Access to the peritoneal cavity may be achieved with Veress needle insufflation and blind trocar placement ('closed technique'), or an open incision through the fascia, with placement of a blunt Hasson trocar under direct vision ('open technique'). Newer optical access trocars incorporate a laparoscope into the initial trocar so the path of access may be visualized. All three techniques are widely used, but open access has a slightly lower complication rate in large retrospective series.<sup>7,8</sup> However, smaller prospective randomized trials have not shown a difference in major complications between closed-access and open-access techniques.<sup>9</sup> Optical access has not been as widely evaluated as the other two techniques, but may be safer than closed access, since the path of access is visualized.<sup>10,11</sup> Nevertheless, there are reports of bowel injury with the use of optical access trocars. Access-related complications most commonly involve preperitoneal insufflation, injury to visceral vessels or bowel, and abdominal wall hemorrhage.

Preperitoneal insufflation occurs if the Veress needle is placed superficial to the peritoneal cavity. Limited insufflation of this potential space results in the peritoneum

being pushed away from the abdominal fascia, and may make subsequent trocar placement difficult. One indicator of preperitoneal insufflation is high pressure at low volume of insufflated carbon dioxide. If a trocar is placed, preperitoneal fat will be visualized, and the abdomen may appear asymmetrical. Management of this complication usually necessitates open trocar access with a direct cutdown into the peritoneal cavity. Preperitoneal insufflation also may result in significant subcutaneous emphysema. Finally, the peritoneal space may not fully expand after proper access is achieved, thus limiting visualization in portions of the operative field. Preperitoneal insufflation can be avoided by performing a 'drop test'; saline is injected into the Veress needle, and if it freely flows into the abdomen under gravity, the Veress needle is most likely properly placed. However, this test is not perfect, and the pressure and flow monitors should be closely watched during initial insufflation. If high pressure and low flow are achieved at low volume, then the Veress needle is likely not placed properly, and preperitoneal insufflation is a possibility.

Major vascular injury during access must be recognized immediately in order to avoid catastrophic sequelae. Vascular placement of the Veress needle is apparent when aspiration reveals blood in the syringe. Although the needle can be safely withdrawn in many cases, some instances have required open surgical repair, and death has been reported from an aortic puncture.<sup>12</sup> An alternative is to leave the needle in place, and directly examine the puncture from an access point. The needle can be withdrawn under direct vision, and appropriate hemostatic measures can be instituted. If a major injury is suspected, laparotomy should be performed. Laparoscopic vascular repair is possible, but should be undertaken only by an experienced surgeon.

Trocar injury to the aorta, vena cava, or major pelvic vessels may occur during access. Brisk blood return will be noted with removal of the obturator or during laparoscope insertion. The obturator should be returned to the cannula to tamponade the hemorrhage. Immediate laparotomy should be considered, and the trocar should be left in place as it can guide the surgeon to the site of injury. The laparoscopist may need the assistance of a vascular specialist to obtain control of the injured vessel, and the anesthesiologist should be active in resuscitation of the patient. If the trocar has been displaced from the injury, the laparoscope may be inserted into the abdomen to visualize the site of hemorrhage. Nevertheless, laparotomy should not be postponed in patients with major vessel injury from trocar placement, as these patients have substantial morbidity and mortality.<sup>13</sup> Delayed recognition has been reported several times, as the injury may be outside of the operative field, or hemorrhage may be confined to the retroperitoneum or pelvis.<sup>14,15</sup>

The Veress needle may also be placed into the small or large intestine. Upon aspiration, enteric contents may be noted in the syringe. Access should be made at a second site, and the area can be inspected for enteric leak. If necessary, the injury can be oversewn laparoscopically, or if a large defect is noted, laparotomy and formal repair may be needed. If the misplaced Veress needle is not recognized, insufflation of the bowel will reveal high pressures at low volumes. Flatus or asymmetrical distention of the abdomen may be noted. In patients with suspected abdominal adhesions, an open-access technique may be used to minimize this complication.

Trocar injury to the bowel requires repair. Upon insertion of the laparoscope, the inner mucosa of the bowel may be visualized, thus securing the diagnosis. Injury may also be noted after insertion of the secondary trocars, revealing more extensive injuries on the

path of the initial access port. Laparotomy for repair of the injury may be necessary. The entire bowel should be examined circumferentially, as 'through and through' injury may have occurred. Laparoscopic repair of an isolated injury is possible for surgeons experienced with intracorporeal suturing or stapling.

Abdominal wall injury during access may be a cause of hemorrhage. The most significant vessels causing this complication are the inferior epigastric vessels, which may be injured from lateral trocar placement. Usually, a constant dripping of blood from the trocar indicates injury to abdominal wall vessels. A hematoma may develop at the site of injury. Transillumination of the abdominal wall will help to avoid superficial vessels, but the inferior epigastric pedicle usually will not be seen.

The epigastric vessels usually lie at the margin of the rectus sheath, and trocars should be placed lateral to this site. Handheld intraoperative ultrasound has been used to localize the epigastric vessels intraoperatively with great success, but may not be practical in most cases.<sup>16</sup>

If abdominal wall hemorrhage is suspected, the area should be inspected externally and laparoscopically. The bleeding vessel can be cauterized if it is visualized. If not seen well, a variety of suture techniques can be used to control the hemorrhage. The Carter-Thomason fascial closure device (Inlet Medical Inc., Eden Prairie, Minnesota) can be used to create circumferential control of the vessel. Alternatively, a Keith needle may be passed through the skin on one side of the vessel. The needle is grasped with laparoscopic forceps, guided back through the skin and around the vessel, and tied over a bolster. If suturing is not possible, a Foley catheter can be passed into the site, inflated, and retracted against the abdominal wall, thus tamponading the vessel. This technique is probably safe for small venous tears, but control of arterial bleeders may be variable. Importantly, all port sites should be examined at the conclusion of the operation as the trocars are withdrawn. A trocar may occlude a torn vessel, which may reopen upon withdrawal of the trocar from the port site. Newer radially dilating and nonbladed trocars may reduce the incidence of abdominal wall injuries, but further studies need to confirm these theoretical benefits.<sup>11,17</sup>

### *Gas embolism*

Gas embolism is a rare but devastating complication. Although CO<sub>2</sub> is currently the insufflant of choice because of its high solubility in blood, gas embolism may still occur with its use. Embolism commonly occurs in initial access, during which a punctured vein is insufflated. It may also occur at high intraperitoneal pressure, as gas maybe forced into an open vein. Gas embolism is usually recognized when there is rapid cardiovascular collapse. Signs of this complication include a mill wheel murmur, bradycardia or arrhythmia, mydriasis, decreases in oxygen saturation, hypotension, or arrest. End-tidal CO<sub>2</sub> is classically decreased, but may be increased with smaller emboli.<sup>18-20</sup>

Gas embolism occurs when a CO<sub>2</sub> bolus enters the peripheral venous circulation, passes through the right ventricle, and obstructs the outflow of the right heart. These events lead to a decrease in circulatory flow to the left ventricle, decreased cardiac output, and profound cardiovascular collapse.<sup>19,20</sup> Emergent treatment of this complication is necessary; the patient should be placed in the left lateral decubitus position with the head down. Cardiopulmonary resuscitation with appropriate pressors is

often necessary, and an attempt may be made to percutaneously aspirate the embolus by guiding a central line into the right heart. Several deaths have been reported from gas embolism, and vigilant cardiac monitoring during the procedure is essential to recognition of this entity.

Gas embolism may also occur with the argon beam coagulator. This instrument is often used during laparoscopic partial nephrectomy to assist with hemostasis of the incised renal parenchyma.<sup>21–24</sup> The flow rate of the argon beam coagulator may be as high as 6 liters/min, often forcing pneumoperitoneum pressures above 40 mmHg. This high-pressure environment, coupled with actively bleeding venules, can produce an environment in which argon embolism is conceivable. Additionally, argon is 17× less soluble than carbon dioxide. Avoidance of this complication centers on maintaining safe pressures during argon beam coagulation. The CO<sub>2</sub> insufflant may be turned down to lower pressure, and most importantly, a vent can be opened on a trocar to permit rapid gas escape. If argon embolism does occur, treatment is similar to that for CO<sub>2</sub> embolism. Cardiac arrest and death have been reported with the device.<sup>25–27</sup>

### **Complications related to the pneumoperitoneum**

The pneumoperitoneum can alter the patient's physiologic homeostasis. Since the detailed physiology of the pneumoperitoneum is covered in a previous chapter, only the major adverse consequences will be discussed here. As most of the complications are pressure dependent, the laparoscopist should attempt to use the lowest pressure possible during the operation. Most surgeons work between 10–15 mmHg, with higher pressures used transiently to limit bleeding in the field.

The cardiodepressant effects of the CO<sub>2</sub> pneumoperitoneum are well documented.<sup>28,29</sup> Patients generally will experience increased vascular resistance, impaired venous return, and decreased cardiac output. Although these changes may not affect the otherwise healthy individual, patients with compromised cardiac function may be sensitive to these effects, particularly at higher pressures. Patients with severe cardiac dysfunction may require invasive monitoring with central venous catheters or Swan-Ganz lines.

Transperitoneal absorption of CO<sub>2</sub> can lead to hypercarbia and acidosis.<sup>28,29</sup> Usually this effect is countered by increasing minute ventilation; however, patients with impaired pulmonary function or obstructive pulmonary disease may not compensate. Generally, lowering the CO<sub>2</sub> pressure can counter the hypercarbia. In severe cases of hypercarbia, the insufflant may be changed to helium, thus eliminating the insulting agent. Helium, however, is markedly less soluble than CO<sub>2</sub>, and gas embolism is an inherent risk.<sup>30,31</sup> Nitrous oxide may also be used as an insufflant, and has little effect on end-tidal CO<sub>2</sub>.<sup>32</sup>

Urine output is suppressed during laparoscopy,<sup>33</sup> primarily because of decreased renal vein flow and compression of the renal parenchyma. Compression of the ureter has not been implicated, as stenting the patient will not increase urinary flow. The oliguria resolves after the procedure, and no long-term adverse sequelae are known. It is imperative that the anesthesia team be aware of this effect and avoid overhydration of the patient.

The medical effects of the pneumoperitoneum can last for several hours after the procedure ends, as acid-base and ventilatory changes must normalize. Patients with

medical comorbidities should be observed closely in the postanesthesia unit for potential medical complications from the laparoscopic procedure.

### **Electrosurgical injury**

Unlike open surgery, laparoscopic surgery requires the increased use of energy sources to perform tissue/organ ablation. Complications from the use of electrosurgery may arise in this unique operating environment.

Monopolar energy is commonly used in laparoscopic surgery, and a basic understanding of electrosurgical physics is essential to avoiding complications from this energy source. Monopolar energy is transmitted as a complete circuit; the electricity originates at a generator, travels through the surgical instrument to the target tissue, and then spreads over surrounding tissue to the abdominal wall, where a grounding pad re-establishes a connection to the generator. Any break in this electrical loop can injure tissue at the point of disjunction. One mechanism of injury is an insulation defect in the surgical instrument, leading to energy transmission at the leak point. When an insulation defect occurs and cautery use is attempted, energy transmission will not be seen on the target tissue. Instead, the energy will be transmitted at the leak point. The instrument should be withdrawn immediately, and tissues in the path of the instrument should be examined for electrosurgical injury. The device should be closely examined for cracks and insulation defects.

Direct coupling can also cause electrosurgical injury. In this case, another instrument is in contact with the electrosurgical instrument and current is transmitted to the secondary device. Importantly, this contact between instruments may occur outside the field of view. To avoid direct coupling, trocars and instruments should be separated at a reasonable distance, so that the instruments are prevented from crossing or touching. Of note, direct coupling may occur over metal clips or staples; most newer clips are titanium, but the patient may have metallic clips from a previous procedure.

A rare mechanism of electrosurgical injury occurs secondary to capacitive coupling. This injury occurs if the current cannot be transmitted back to the abdominal wall. Such a situation arises with hybrid cannulae, in which the metal shaft of the trocar is anchored to the skin with a plastic apron. The cannula can accumulate electrical energy, which will be transmitted upon contact with tissue or another instrument. With modern access devices, this complication has not been reported.

Electrosurgical injuries may be limited by using alternative energy delivery systems. Bipolar energy is transmitted through an instrument in which the active electrode and the return electrode are in close proximity. Only the area between the electrodes receives the electrical current; there is not a complete electrical circuit through the patient. The most commonly used instruments can also function as forceps or graspers. An alternative energy source is the harmonic scalpel, which utilizes ultrasonic energy.

Although electrical injuries can be minimized with alternative energy devices, none of these devices is protective against a direct organ insult. All energy sources may directly injure bowel or vascular structures during dissection if they are inadvertently fired in close proximity to the naive tissue. Vascular injuries are usually readily apparent, and can

be controlled laparoscopically with sutures or hemostatic tissue sealants. Bowel injury may not be apparent, and surgeons should maintain a high clinical suspicion.

### **Unrecognized bowel injury and management**

Bowel injury may occur at numerous points in any laparoscopic procedure. Bowel may be inadvertently injured during access, dissection, removal or introduction of instruments, and closure. A review of the literature suggests that 69% of injuries are unrecognized at the time of initial laparoscopy.<sup>34</sup> Intraoperative diagnosis may be suggested by blanching of the enteric surface or serosal tears. If a small enterotomy is noted, intraoperative laparoscopic repair is reasonable with intracorporeal suturing. The bowel should be closely examined for multiple injuries, especially if trocar injury is suspected. Bowel resection and reanastomosis is also possible via intracorporeal technique, or extracorporeally through extension of a port site. Open repair should be performed if laparoscopic repair is not feasible.

If unrecognized intraoperatively, the postoperative diagnosis of bowel injury can be difficult. Traditionally, patients with bowel injury present predictably and rapidly with leukocytosis, peritoneal signs, fever, and sepsis. However, laparoscopic bowel injury may not follow this dogma; the presentation is frequently atypical and delayed. The mean time to recognition of bowel injury is 2–4 days after the insult, and may be as late as 2–4 weeks after surgery. Furthermore, patients commonly present with pain at a trocar site, abdominal distention, leukopenia, and diarrhea. Computer tomography (CT) scan can aid in diagnosis, and most patients should undergo open exploration.<sup>34</sup> Mortality is considerable, and may be increased in patients with duodenal injury.<sup>35</sup> After exploration, patients may require intensive care support and parenteral nutrition. Despite the rare occurrence of bowel injury, the clinician should maintain a high level of suspicion for the injury, as the sequelae may be devastating.

### **Port-site metastases**

Laparoscopic surgery is becoming a prevalent treatment modality for various genitourinary malignancies. Therefore, prevention of port-site metastases is necessary to maintain favorable oncologic outcome. The incidence of port-site metastasis after genitourinary oncologic surgery appears to be low; there have been two reports of seeding after radical nephrectomy for renal cell carcinoma and three reports of seeding after treatment of transitional cell carcinoma.<sup>36–39</sup>

The two cases of port-site metastases from renal cell carcinoma are instructive. In one case, the final tumor was a high-grade T3 lesion with sarcomatoid elements. The recurrence of such a tumor at a port-site is analogous to the general surgical literature, in which aggressive cancers such as cholangiocarcinoma have a high rate of port site metastases.<sup>40</sup> The second case occurred after morcellation of a specimen in a patient with ascites; multiple port-site metastases were noted on follow-up. It is unknown if tumor cells were seeded into the ascetic fluid during the dissection or morcellation. These two cases suggest that contamination must be avoided upon specimen extraction. If the

surgeon prefers morcellation, an impermeable tear-proof sac should be used, the field should be doubly draped to prevent exposure of the port site to the specimen, contaminated instruments should be removed, and gloves should be changed at the conclusion of the procedure. The port site should be irrigated thoroughly with heparinized saline. Care is paramount in patients with ascites, as the fluid may transmit the tumor cells throughout the peritoneum.

### **Port-site hernias**

Herniation of bowel or omentum through the trocar sites is a recognized complication of laparoscopy. Generally, 10 mm trocar sites are closed at the fascia level, whereas 5 mm trocar sites are not. In children, 5 mm trocar sites should be closed because they are more prone to development of hernias. Even though most investigators do not close the 5 mm site in adults, there have been rare reports of bowel and omental herniation through the 5 mm site.<sup>41-43</sup> If the 5 mm site is used extensively, the fascia could be weakened, and closure may be favored; ultimately the decision to close these sites is individualized.

New radially dilating trocars make a smaller fascial defect than bladed trocars, and some advocate not closing the 10 mm trocar site if these newer devices are used. These trocars make a fascial defect of 6–8 mm with a 10/12 mm trocar, and the overlying muscle is split instead of incised. Preliminary studies of the radially dilating trocars have not reported herniation, but longer-term and larger studies are needed to verify this outcome.<sup>44,45</sup>

### **Individual procedures**

Since the first laparoscopic nephrectomy was described by Clayman et al in 1991, surgeons have expanded the use of laparoscopy to several other procedures.<sup>46</sup> Several series have documented the efficacy and safety of operations that were traditionally performed with open techniques. The following sections will review complications which are salient to the more commonly performed laparoscopic urologic procedures. These include nephrectomy (donor, radical, partial, simple), nephroureterectomy, pyeloplasty, adrenalectomy, retroperitoneal lymphadenectomy, and prostatectomy. Most of these procedures have complications which mirror their open counterparts, but laparoscopic management is possible in several instances.

#### *Donor nephrectomy*

One unique complication that has been encountered in laparoscopic donor nephrectomy compromises ureteral complications in the recipient. Two groups reported an increase in ureteral complications in their initial experience. Technical modifications have been made to successfully minimize this complication. The ureteral dissection is very limited to preserve the vascular supply to the structure; no dissection is performed lateral to the gonadal vein. The gonadal vein and ureter should be harvested in one large bundle of

tissue. This alteration has decreased the ureteral complication rate from 10% to 3%, which is similar to rates in open series.<sup>47,48</sup>

### *Radical nephrectomy*

Major complications occur in 3–8% of laparoscopic radical nephrectomies.<sup>49–54</sup> Hemorrhage is the most common major complication, and can be controlled with pressure from sponges, identification of the bleeding vessel, and selective use of suture, cautery, fibrin glue, or clips. Conversion to a hand-assisted operation or open operation can also aid in control of bleeding. Other reported complications include injury to the superior mesenteric artery, diaphragmatic injury, pancreatic fistula, and splenic injury.

Dissection of the upper pole of the kidney can result in a diaphragm injury. A small rent may not be apparent, but the anesthesiologist may note an increase in pCO<sub>2</sub>. These injuries have been repaired with intracorporeal suturing, synthetic meshes, and tissue glue.<sup>55–58</sup> A residual pneumothorax may be aspirated or a chest tube may be placed to allow lung inflation.

### *Radical nephroureterectomy*

Major complications occur in 8–12% of cases, and hemorrhage is the major cause of conversion.<sup>59–63</sup> Complications may also occur secondary to the management of the distal ureter. There are many methods to resect the distal ureter and intramural tunnel; however, retroperitoneal recurrence has been reported after using the ‘pluck’ technique.<sup>64</sup>

### *Partial nephrectomy*

Laparoscopic partial nephrectomy is an emerging technique, and can be reasonably undertaken by experienced laparoscopists. In most series, the patients are highly selected, as peripheral and exophytic lesions are more amenable to excision than central or large tumors. In the largest published series, Gill et al note that only 20% of their institutions’ partial nephrectomies are approached laparoscopically.<sup>65</sup> Complications occur in up to 20% of patients, and predominantly include hemorrhage and urine leak.<sup>65–67</sup>

Hemorrhage may be controlled intraoperatively by suturing of the parenchyma, fibrin glue, argon beam coagulation, and/or preoperative ablation with radiofrequency energy. Vascular clamping is an option, as is hand assistance. Ultimately, if these adjunctive measures fail to control hemorrhage, the operation may be converted to an open procedure or to a laparoscopic radical nephrectomy. Postoperative hemorrhage has also been reported and patients can be stabilized with transfusions. Embolization of bleeding vessels or re-exploration should be considered.

Urine leak may occur even if the collecting system appears to be adequately closed. Hemorrhage in the renal bed may also damage the suture line and contribute to collecting system openings. Leaks can be identified intraoperatively by placing an external stent and injecting saline or indigo carmine into the collecting system. Alternatively, leaks may be detected with direct visualization of the collecting system under laparoscopic magnification. A drain should be placed in the retroperitoneum to evacuate excess fluid and prevent urinoma. If a urine leak develops, continue suction drainage for 7–10 days to



create a controlled fistula. Then, the drain is taken off suction, and can usually be removed in 48 hours. If a large symptomatic urinoma is present, it may be percutaneously drained.

### *Laparoscopic pyeloplasty*

The major complication has been urinary leakage and ascites, secondary to drain migration.<sup>68</sup> This occurred in 2% of patients in the largest series. This complication may be avoided by placing the drain posterior to the line of Toldt, and posterior to the repair.

### *Simple nephrectomy*

A simple laparoscopic nephrectomy may be more difficult than a radical nephrectomy if the patient has had multiple episodes of pyelonephritis. Tissue planes may be indistinct because of inflammation and scarring. Particular caution is advised in patients with xanthogranulomatous pyelonephritis, in whom the complication rate is very high, and open conversion is required in more than 50%.<sup>69,70</sup>

### *Adrenalectomy*

A recent review of publications reporting 50 series of laparoscopic adrenalectomy revealed bleeding as the most common complication of laparoscopic adrenalectomy.<sup>71</sup> This complication is more common in the early experience. Bleeding may arise from the renal vein, adrenal vein, vena cava, or renal artery branches. Bleeding also accounts for 30% of conversions. The overall transfusion rate of 2.8% is similar to that in open series. Laparoscopic reexploration for hemorrhage has been successful in 6/7 patients in the reported series.

### *Retro peritoneal lymph node dissection*

Hemorrhage is the major complication of laparoscopic retroperitoneal lymph node dissection for stage I nonseminomatous germ cell tumors.<sup>72-78</sup> Reports of hemorrhage from the vena cava, renal vein, lumbar veins, and gonadal vein have been reported. In most cases hemorrhage can be controlled with pressure, clips, tissue glues, and/or suturing, but conversion should be considered if laparoscopic repair is difficult. The overall conversion rate ranges from 2.6% to 6.9%.

Postchemotherapy laparoscopic retroperitoneal lymph node dissection carries a much higher complication rate than primary lymph node dissection; a similar situation is seen with the corresponding open procedures.<sup>79,80</sup> In one series chylous ascites occurred in 21% of patients, but resolved in all patients with dietary adjustments. In another series, major complications occurred in 42% of patients, with renal vascular injury being a major cause of morbidity.

### *Radical prostatectomy*

Radical prostatectomy is a challenging laparoscopic procedure, and should be undertaken by an experienced team with intracorporeal suturing abilities. The overall complication rate is 8.9–18.8%. Conversions occur more commonly in the initial experience, and range from 1.2% to 4.4%. Major intraoperative complications include rectal and bowel injury, anastomotic leak, pelvic or intraperitoneal hematoma, and bladder or ureteral injury. Longterm data on potency and continence are still pending.<sup>81–86</sup>

Hemorrhagic complications usually arise from the dorsal venous complex or the prostatic pedicles.<sup>86</sup> The dorsal venous complex can be visualized closely and oversewn or cauterized if necessary. The technique of hemostasis on the pedicles may vary, depending upon the indications for nerve sparing. If nerve sparing is used, the estimated blood loss of the procedure may be increased, and precise vascular control with the bipolar instrument is recommended. A rare cause of hemorrhage is an epigastric artery injury from a trocar site. Care should be taken to inspect the lateral trocar sites for bleeding, particularly at the time of closure.

Rectal injury may occur during the posterior dissection of the seminal vesicles, or during the apical dissection if Denonvilliers' fascia has not been adequately separated from the apex.<sup>86</sup> Although a rectal bougie may aid in identification of the rectum, it cannot absolutely prevent injury. If recognized intraoperatively, rectal injury can be sutured laparoscopically. However, laparotomy and diversion should be considered in the event of fecal contamination or large injuries.

Bowel injuries have been missed intraoperatively during this operation, and may be related to transmission of current or direct injury from replacement of instruments. As previously stated, presentation may be atypical. General surgical consultation is indicated, and laparotomy is usually necessary.

Ureteral injury may occur if the ureter is mistaken for the vas deferens. Lateral superior identification of the vas can prevent this complication. Ureteral necrosis has also been noted with extensive mobilization of the bladder to release it from the peritoneum. Unrecognized injury may be manifested in urinary ascites and elevated creatinine.

Vesicourethral anastomotic leak occurs in up to 10% of patients.<sup>81–86</sup> Patients may develop an elevated serum creatinine as a result of intraperitoneal urine absorption. Most patients exhibit high pelvic drain output. Decrease of fluid intake, verification of Foley catheter position, and continued drainage have been successful in most cases.

Urinary retention may develop when the Foley catheter is removed on postoperative day 1 or 2. By postoperative day 4, the incidence of this complication is <5%.

### **Summary**

To minimize complications of urologic laparoscopic procedures, the surgeon should understand laparoscopic physiology and should be experienced with specialized surgical instrumentation. Although complications are of a frequency similar to that of open surgery, the recognition and management of many complications differ. The informed

and experienced surgeon can decrease complications and effectively deliver the advantages of minimally invasive urology.

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# Robotic tools for minimally invasive urologic surgery

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## Introduction

Surgical robots have begun to appear on the market in the last few years and have started to populate the operating rooms in large medical centers. These systems have already established their ability to augment a surgeon's dexterity in minimally invasive procedures and have the potential to improve patient outcome, even though, for the moment, their cost is prohibitively high for widespread application. As surgeons become increasingly aware of the clinical benefits of these systems and costs are driven down by technological advance and availability, we foresee that robots will become standard operating room tools. Initial use of a handful of robots has already demonstrated their surgical potential. As technology evolves, robots may not only improve performance in minimally invasive procedures but may also enhance the performance of other existing procedures or even make possible entirely new kinds of operations.

This chapter outlines the current capabilities and limitations of several commercially available and experimental surgical robots. Local and telesurgical systems and procedures are discussed together with a forecast of future development. We provide an overview of surgical robotic technology, terminology, and classification, as well as a short history of their evolution, highlighting the potential of these systems, before proceeding to discuss several specific surgical systems.

## Overview of surgical robotics

Computer-integrated surgical systems are a new class of 'intelligent' surgical tools which may include surgical robots. The robotic manipulator itself is just one element of a larger system that includes preoperative planning based on medical images, intraoperative registration (matching the patient to the presurgical images) and a combination of robotically assisted and manually controlled tools for carrying out the plan, as well as patient verification and follow-up.

The chief advantages of robotic manipulation of surgical tools are generally:

- accurate registration of patient's body to medical images
- consistent movement, free of fatigue and tremor
- the ability to work in imaging environments unfriendly to human surgeons
- the ability to reposition instruments quickly and accurately through complex trajectories or onto multiple targets.

In surgical robotics the task may either be predefined by the surgeon based on preoperative/interventional data or, for more complex procedures, be defined as the surgery progresses in the operating room. On the basis of this distinction, surgical robots may be classified into two main groups: image-guided and surgeon-driven systems. These categories both make use of the complementary skills/advantages of the surgeon and the robot, but they do so in different ways.

Image-guided robotic systems excel at precisely reaching a target specified by the surgeon. In radiologic interventions such as percutaneous needle access, these systems are used to guide and sometimes to insert a needle, instrument, or probe. Their purpose is to act as a trajectory enforcement device, correctly aligning the needle based on images from ultrasound, C-arm or biplanar fluoroscopy units, computed tomography (CT) or even magnetic resonance imaging (MRI) scanners.<sup>1</sup> Image-guided systems take advantage of the capability of robotic systems to register the medical image to the patient more easily and accurately than humans can. The robot can then precisely manipulate instruments to reach the locations in the patient space that are selected in the medical image. The system complements the planning and decision-making skills of the surgeon by actualizing his intention.

With surgeon-driven robots, the surgeon directly controls the motion of the instruments held by the robot. These systems combine the fine manipulation capabilities of robotic systems with the surgeon's perception and judgment, performing scaled-down, steady, tremor-free motion. These robots enable increased resolution of movement and vision, and make laparoscopic tools more dexterous. The laparoscopic robot 'hands' emulate the movement capability of human hands and wrists much better than do the traditional laparoscopic tools. Additionally, robotic systems can fuse radiographic and three-dimensional (3D) data to realtime surface data, providing better visualization of the target tissue or structures that need to be avoided.

When performing surgery with a robotic system, the surgeon is often located distal to the operating field. Robotic tools allow easier access to confined spaces in minimally invasive procedures and also enable the doctor to be at a distance from the patient and, thus, perform telesurgery.<sup>2</sup> Future developments may allow the computer to sense joint and muscle movements in the operator's hands, arms, head and neck, and to respond accordingly. A prototype system currently under development senses the electrical signals in the operator's biceps, and flexes or extends a robotic arm accordingly.<sup>3</sup> Increased public demand for minimally invasive surgery is not being satisfied by a sufficient number of experienced, qualified surgeons.<sup>4</sup> Telemedicine provides the unique advantage of allowing specialists in remote locations to assist and train local surgeons. Robotic tools enable the remote surgeon not only to offer advice but also to participate directly in the operation. This has been successfully done intercontinentally, as described later.

Robotic systems have profound implications when applied to training. Robotic and computer training simulations can enable some surgical training activities to be carried out in virtual reality or simulated environments without risk and/or harm to an animal or human patient. Further, these devices may one day allow surgical learning progress to be measured quantitatively and tracked over time.

Robotic surgery is a fascinating and quickly evolving field of medicine as doctors and engineers collaborate to develop innovative new procedures and the technology that



makes them possible. While patients will grow to appreciate the accuracy of robots, they will always want the judgment of a human doctor in control of the robot. Robotic technology will never replace the doctor, but it represents a new type of tool with promising capabilities.

### **History of urologic robots**

Robotic-assisted devices in medicine were first used in rehabilitation before making their way into the operating room.<sup>5</sup> Surgical robotics pioneered in the 1980s in the fields of orthopedics and neurosurgery with predefined task robots.<sup>6</sup> Because of the difficulty of building robots to operate on soft tissue organs with their higher deformability and mobility, urology robotics (URobotics) was slower to develop. Although these difficulties delayed development of URobotics, innovative research has produced several systems either applicable to, or purposely designed for, urology.

The first URobot was the PROBOT, introduced in 1989 by a group at the Imperial College in London for performing robot-assisted transurethral resection of the prostate (TURP).<sup>7,8</sup> The robot serially cored the periurethral prostatic tissue, while hemostasis was achieved manually using electrocautery after completion of the tissue resection. The device never achieved widespread use; however, since then, many minimally invasive techniques for the treatment of benign prostatic hyperplasia have been introduced, thus confirming the desire to replace the standard TURP with a less-invasive strategy. Transrectal ultrasound (TRUS) is used in many of these new techniques for intraoperative monitoring and image-guided robot assistance.

In 1994, Potamianos et al investigated a robotic system to assist the urologist with intraoperative percutaneous renal access.<sup>9</sup> They employed a passive, encoded arm equipped with electromagnetic brakes, mounted onto the operating table. The access needle was manually positioned as prescribed by a computer, which triangulated the calyx location from multiple C-arm X-rays.<sup>10</sup> In-vitro experiments evaluating system performance demonstrated a targeting accuracy within 1.5 mm or less.

In 1995, a research group headed by Russell Taylor at IBM developed the remote center of motion (RCM) concept and implemented it on the LARS robot.<sup>11,12</sup> The RCM is a component of nearly all medical robotic systems today. LARS was used in our institution for experimental percutaneous renal access.<sup>13</sup> These experiments revealed areas for improvement and led our URobotics research group to create the PAKY-RCM (Percutaneous Access of the Kidney) robot.<sup>14</sup>

The use of robots in laparoscopy is yet another step in the evolution of minimally invasive techniques and has been successfully applied in several centers in Europe and the USA. The first robots used to control laparoscopic tools in urologic surgery were manipulator arms such as the Automated Endoscopic System for Optimal Positioning (AESOP; Computer Motion, Inc., Goleta, California). Such laparoscopic systems are quite recent, having been developed in the late 1990s and cleared by the FDA (Food and Drug Administration) within the past few years.

The entire history of robots in surgery is rather short, but in this brief period, the technology has matured sufficiently to prove its worth. Systems developed thus far seem

to be adaptable to specific architectures and characteristics imposed by the stringent surgical environment.

### **Common components of surgical robotic systems**

Perhaps the most important and specific component of the surgical robot is the manipulator. Surgical manipulators are electromechanical arms equipped with sensors and actuators responsible for holding and precisely moving the surgical instrument under computer control. The most common kinematic architecture of surgical manipulators has thus far been the RCM, which is a specific characteristic of surgical robots as opposed to industrial types.

The RCM is a mechanism used by the surgical manipulator to enable and facilitate the pivoting motion of instruments about a fixed point in space, normally located on the instrument itself. This mechanism enables minimally invasive instruments to preserve a consistent entry point, or port, throughout the entire procedure. This technique was developed by observing the surgeon's natural motion in manual laparoscopy. The RCM is a mechanism that accomplishes the same task. Following the insertion of the instrument, the RCM causes it to pivot about a fixed point in space—the point where it enters the body. Different robots use more or less sophisticated means of implementing the RCM, but there are very few surgical systems not using this principle today. In fact, all commercially available surgical robots are RCM-based robots.

Another important general component of medical robotic systems is the image acquisition device. This may generally be any medical imaging device (video, infrared, ultrasound, X-ray, or MRI), although imager compatibility issues exist, especially for the class of MRI scanners. Minimally invasive surgery utilizes intraoperative video and/or infrared cameras to provide the surgeon with a view of the surgical area. Since laparoscopy is highly dependent on the quality of the image the surgeon sees, there has been considerable recent attention paid to progress in optimizing laparoscopic imaging. Presently in use, stereo endoscopes allow for 3D visualization of the surgical field.<sup>15</sup> This increases surgical performance by facilitating more precise dissection between delicate anatomical planes and razor-sharp precision when handling sutures and minute tissue layers.<sup>16,17</sup> Unfortunately, many of the current technologies for 3D imaging are bulky and difficult to use. High-definition (HD) imaging is now available, although not in widespread use. HD camera chips produce more than 2 million pixels of resolution (or approximately 4 times better than the best traditional camera chips). It is estimated that the current cost of a complete HD video system for the operating room ranges between US\$250,000 and US\$500,000.<sup>15</sup> Although cost presently prohibits many laparoscopic centers from using HD technology, as the technology matures and costs drop, it is only a matter of time before HD technology becomes standard operating room technology.

The computer is the third general component of the surgical robotic system. Surgical robots bring computers into the operating room in a new way, providing a link between the 'data world' of medical images, sensors, and databases, and the physical world of surgical actions. This combination makes it possible to plan and execute surgical interventions precisely and predictably by fusing real-time and presurgical information about the patient. This information can then be used to improve surgical decision making

and real-time control of surgical instruments. As robotic systems continue to incorporate real-time control and sensing, interventions will become more consistent and accurate than freehand interventions.

Furthermore, the computer inherently has the ability to acquire and retain a great deal of information about each intervention. For example, how much force was applied? For how long? Where, exactly, was a suture placed? Many such questions have yet to be quantitatively understood. Currently, the analysis of such log data attracts a good deal of attention within the medical robotics research community. As research progresses, we expect that lessons will be learned and additional experience will be acquired by surgeons through the use of these new 'smart' tools. This will, in turn, improve surgical quality and outcomes, in much the same way that similar uses of data have improved manufacturing quality and flight safety.

### **Image-guided robotic systems**

The idea behind image-guided robotic systems is to allow the surgeon to 'point and click' on a medical image of a location within an organ, approve his or her selection and cause a robot to place a tool (a needle for example) at the physical equivalent of the position selected on the medical image. The first example of such a system was the work of Potamianos et al described previously.

The Johns Hopkins URobotics Laboratory<sup>18</sup> has developed several robotic components for image-guided percutaneous access. PAKY is an active and radiolucent needle driver.<sup>19</sup> Originally held by a passive arm, the needle in the needle driver was manually positioned under C-arm guidance. It was then locked in place and the needle inserted automatically under the surgeon's joystick control.<sup>20</sup> The next step was automation of the needle orientation procedure, which was accomplished with the addition of the RCM module.<sup>14</sup> The RCM supports and orients the PAKY driver while maintaining the fixed location of the needle tip. The combination of the two robotic systems enables the surgeon to place the needle automatically at a target specified on the computer screen by the urologist, on the basis of fluoroscopic images.<sup>21</sup> The PAKY-RCM offers an unquestionable improvement in needle placement accuracy and lowers procedure time while reducing radiation exposure to the patient and the urologist.<sup>22</sup>

Clinically, the PAKY-RCM system was tested in local as well as in several transatlantic telesurgical cases.<sup>23</sup> The PAKY-RCM system was also used under CT guidance with the Laser-Based CT/MR Registration.<sup>24</sup> This method of registering the patient to the image makes use of the laser markers readily available on any CT scanner. Once registered in this manner, the organ of interest can be targeted precisely. The procedure has been successfully used for biopsies and radiofrequency (RF) ablation of targets on the kidney and spine, as well as for nephrostomy tube placements.<sup>25</sup>

The newest robotic system from the Johns Hopkins URobotics Laboratory is called Tracker (Figure 55.1). It is mounted on the CT table and enters the scanner along with the patient.<sup>26</sup> Percutaneous access is achieved in the confined space of the imager without interfering with imager functionality. Tracker has undergone final laboratory evaluations and is now under clinical trial.<sup>27,28</sup>

The imaging method that yields perhaps the best-quality soft tissue images is MRI. Unfortunately, this is also the imaging method most difficult to use with a traditional (metal) robot. The high magnetic fields of the MRI cause forces equal to 27 times gravity on ferromagnetic metal objects, as well as heating them and causing other undesirable effects. Despite these difficulties, there is strong motivation for building an MRI-compatible robot because of the imaging capabilities of this technology. While CT scans are becoming more accurate, even spiral CT cannot provide as much information as MRI for many pathologies and organ systems. Using a CT scan, it is often possible to see small, suspicious areas in the prostate, but have extreme difficulty in accurately targeting them with the biopsy needle while relying on printed images and simultaneous TRUS. It can certainly be frustrating to see a lesion without having the option to locate it outside the scanner. The ideal solution is to be able to perform a biopsy under the real-time guidance of MRI images.

Several research groups are currently examining this problem. One MRI-compatible system for noninvasive surgery has been developed by Hynynen et al.<sup>29</sup> Another MRI-compatible device, a needle insertion manipulator using ultrasonic actuation, has been built by Masamune et al at the University of Tokyo<sup>30</sup> and tested on phantoms. Yet another system is currently under investigation at Brigham and Women's Hospital, Boston, Massachusetts. This is a robot with two long arms that extend into the imaging field by entering the space between sections of a specially designed 'double donut' MRI scanner.<sup>31</sup> The system can be used as an image-guided surgical assistant, integrating preoperative planning and intraoperative MRI images. The Johns Hopkins URobotics Laboratory is also working on a multi-imager-compatible robot with MRI capability for precise prostate access that incorporates a new kind of harmonic and planetary motor.<sup>32</sup> While there is much current research aimed at building MR-compatible robots, there are no clinically applicable systems of this type on the market at the present time.

Another interesting system, under investigation by an Italian group, uses a different strategy to improve the link between medical images and reality. The group have developed and evaluated an ultrasound-guided robot for use in transperineal biopsies.<sup>33,34</sup> This system uses four real-time video cameras and integrates this information with data gathered from the TRUS to position the robot for sample collection. Although the system has demonstrated target accuracy of 1–2 mm, expense and set-up time presently hinder feasibility.

A system for prostate brachytherapy with TRUS guidance is under development in the Johns Hopkins URobotics Laboratory in collaboration with the CISST Engineering Research Center and Burdette Medical Systems, Inc. Recently, a first evaluation has been successfully completed on phantom models<sup>35</sup> (Figure 55.2), and a specifically designed robot, which will integrate with the Burdette brachytherapy stand and dosimetry algorithms, is currently under development. This system will take advantage of advances in ultrasound technology that enable the TRUS alone to be sufficiently precise to hit targets accurately without the need for a cooperative, concurrent imaging modality.



**Figure 55.1** Tracker robot for CT-guided interventions. (Courtesy of Johns Hopkins URobotics Laboratory, Johns Hopkins Medical Institutions (JHMI).)



**Figure 55.2** System for ultrasound-guided robotic brachytherapy. (Courtesy of Johns Hopkins URobotics Laboratory and Burdette Medical Systems, Inc.)

### **Surgeon-driven robotic systems**

In contrast to image-guided robots, which automatically manipulate instruments under the prescription of the physician based on the digital image information, surgeon-driven systems take the surgeon's input continuously and, in real time, translate it to corresponding instrument manipulation. Surgeon-driven robots augment the manipulation capabilities of the physician in ways that passive, classic instruments cannot. They can decrease tremor, scale motion, aid in manipulation of tissues in confined spaces, and have

the potential to provide remote haptic (tactile and force) feedback. They thereby enable decreasingly invasive operations to be performed.

The first surgeon-driven surgical assistant to receive FDA clearance was the AESOP, a robotic, laparoscopic camera holder. The AESOP has six degrees of freedom (DOF), two of which are passive (meaning they are positioned by hand and do not have motors actuating them). AESOP is easily mounted on the operating room table and can be conveniently stored away, mounted on a special cart. The function of AESOP is to hold and orient a laparoscopic camera under hand, foot or voice control.<sup>36</sup> The two passive joints protect against lateral forces on the abdominal wall during camera manipulation.

Perhaps the primary reason for AESOP's success is that it is simple to operate and, at the same time, reliable and safe. Additionally, the robot is easy to disconnect intraoperatively in the (highly unlikely) event that problems should arise. It is routinely used at several institutions and in many surgical disciplines, including a variety of laparoscopic urologic procedures.<sup>37-39</sup> The camera is significantly steadier under robot control and neither operative set-up nor breakdown time is increased with the use of a robotic assistant.<sup>40</sup>

A surgeon-driven system to manipulate instruments designed for open surgery has been developed at the Stanford Research Institute (SRI), Menlo Park, California. The surgeon operates the two-armed robot equipped with high-mobility grippers from a remote console. Bowersox and Cornum have used the system for in-vivo porcine nephrectomies and repair of bladder and urethral injuries.<sup>41</sup>

Perhaps the most successful surgeon-driven robot thus far is the da Vinci Surgical System for laparoscopy (Intuitive Surgical, Inc., Mountain View, California). The system was tested in early 2000 in Europe by cardiovascular surgeons performing laparoscopic cardiac bypass operations without using an extracorporeal cardiopulmonary bypass.<sup>42</sup> The da Vinci Surgical System consists of a three-armed robot connected to a remote surgeon console (Figure 55.3). The surgeon operates the system while seated at the nonsterile console. The vision system is controlled using foot pedals and displays a 3D image of the surgical field similar to that seen in the open surgery case. The surgeon's movements are translated in real time to movements of the pencil-sized instruments in the surgical field. These enter the patient through small ports (on the order of 5–10 mm, depending on the tool). Two of the robotic arms are used for manipulating the surgical instruments, while the third arm manages the laparoscope. The instruments (needle holders, scissors, dissectors, scalpel, etc.) have seven DOF including rotation, and are maneuvered by a robotic wrist.

Using the da Vinci Surgical System, one can potentially bypass much of the long learning curve traditionally associated with minimally invasive surgery. This is because the device automatically orients tool motion with respect to the camera view. Move your hand up and the tool moves up in the image, regardless of whether this lies physically in the same direction. Thus, the difficult, inverted, counterintuitive movements of conventional laparoscopy are eliminated and replaced by natural hand-eye coordination. Also possible is the reorienting of the surgeon's hands to more comfortable positions. With traditional laparoscopic tools, it is sometimes necessary to work with arms uncomfortably contorted in order to reach an object with the tools at the proper orientation. Using the da Vinci Surgical System, the surgeon can move the tools to the proper location and orientation, press a button to hold them in place while he moves his

controls to a comfortable position and then resume control of the tools. The da Vinci Surgical System was cleared by the FDA in mid-2001 and is already in use at many centers throughout the USA in several surgical disciplines. Robotassisted urologic surgery has already been successfully performed for partial/total and donor nephrectomies, pelvic lymphadenectomy, pyeloplasties, cryoablation procedures, diagnosis and treatment of cryptorchidism, as well as for radical prostatectomy and retroperitoneal procedures.<sup>43-47</sup>



**Figure 55.3** AESOP arm (foreground—left) and daVinci Surgical System (background—left, and surgeon's console—right) in a laparoscopic prostatectomy case at Johns Hopkins Medical Institutions (JHMI).

A competitor system is the Zeus system from Computer Motion, Inc., Goleta, California (the makers of AESOP). Similar to the daVinci Surgical System, the Zeus consists of the combination of three robot arms and a surgeon's control console. The system uses one AESOP for the laparoscope and the other two arms hold surgical instruments. Compared to the daVinci Surgical System, Zeus appears safer and requires significantly less preoperative setup. On the other hand, until recently, Zeus had exhibited lower dexterity of the tools within the patient. However, the company seems to have addressed this with the Micro Wrist line of end-effector tools. Zeus received FDA clearance as a general laparoscopic tool in September 2002. The system has been used experimentally in a number of operations, including urology cases.<sup>46,48</sup> Most recently, Dr Peter Schulam at UCLA has used the system for reconstructing the kidney's draining system.<sup>49</sup>

Although very precise, present robotic systems lack the capability of completely reproducing tactile sensation (known as haptics). Some systems, such as Zeus, include partial force feedback,<sup>50</sup> but realistic, general haptic feedback is still a research topic.

While the daVinci Surgical System does have some haptic feedback capability, this is usually disabled when the robot is used, because it does not provide a realistic feel. This is primarily because the forces are sensed from outside the patient, causing forces generated at the port to have a predominant effect, disturbing the sensation of forces experienced at the tip of the instrument. Haptics is an active research topic within the engineering community.<sup>51,52</sup> A good deal of work has been done investigating new kinds of tactile sensors.<sup>53-57</sup> There are also theoretical questions as yet unanswered about how best to display haptic information and there are a number of technical obstacles to overcome in hardware development, signal processing, and systems integration before general haptic feedback will be possible.<sup>56-58</sup>

### **Telemedicine, telementoring, and telesurgery**

The real-time data exchange of medical information between physicians in different locations is known as telemedicine. Telementoring describes the assistance of an experienced surgeon in a remote operation, while telesurgery implies his active involvement in the operation, manipulating instruments through the use of remotely controlled robots. The increasing accessibility of telecommunication systems, ranging from simple telephone lines to high-bandwidth fiberoptic and satellite transmissions,<sup>59</sup> allows physicians to communicate with their peers over any terrestrial distance. Teleconferences, broadcast surgeries, and consultations of specialists are common today, along with the worldwide exchange of medical images and data through the Internet. Surgical teleconsulting has been demonstrated to improve medical decision making, patient outcomes, and medical training.<sup>60</sup> Instead of being forced to travel long distances to other countries, specialists can now be available at any desired location for conferences or meetings while they sit at their office desks. Telemedicine has been successfully carried out over long distances between hospitals in the USA and Europe. Initial reports of telementoring and telesurgery were published as early as 1994 by Kavoussi et al.<sup>39,61</sup> and followed by a variety of intercontinental operations.<sup>62-68</sup>

In most cases, the surgeon remotely operated one or two robots, assisting the surgical team at the local hospital. The surgery begins with the local team setting up the operation: inserting the trocars and positioning the robots. Then, the remote surgeon controls only the laparoscope held by the robot to obtain a view of the surgical field. He also, in some cases, uses a telestrator to illustrate incision lines, anatomic structures, or critical areas visually to the local team.<sup>69</sup> The lag times for transmission of data have all been reported to be less than 200 ms and are hardly noticed during the procedure.<sup>61,69,70</sup>

By using an additional robot like the PAKY-RCM, the remote surgeon can actively retract organs or insert needles. The first transatlantic, assisted telerobotic surgery using two robots was successfully performed between Baltimore, Maryland, and Munich, Germany, in April 2001.<sup>71</sup> The remote surgeon controlled the laparoscope from his house via the AESOP robot, as well as a laparoscopic retractor with the PAKY-RCM robot. Active involvement in the operation was achieved by managing the gas inflation, telestration and electrocautery (Figure 55.4). For the transmission of the audio and video signal as well as robot control, a total of 512 kilobits per second (kbps) was needed, delivered by four ISDN lines at 128 kbps each. Although the remote expert was half a



world away from the patient, his active involvement in the operation, along with the live visual and audio displays, gave the feeling of the expert's being in the operating room.

The most profound example of telesurgery thus far is known as Operation Lindbergh. This surgery was carried out using the Zeus robotic system between New York (remote location) and Strasbourg, France (patient location). The procedure was a complete laparoscopic cholecystectomy, and was performed in September 2001. The surgery was carried out by Dr M Gagner (remote surgeon) under the local supervision of Professor J Marescaux, and was a complete success.<sup>67</sup> The event achieved worldwide recognition<sup>63,64</sup> in popular and scientific media.

One of the future goals of telesurgery is to deliver health care in medically underserved areas and thereby limit patient transportation.<sup>65</sup> Additionally, telesurgery has applications in armed conflicts where qualified medical care may not be readily accessible. This scenario was successfully investigated with telementoring via satellite connection between an aircraft carrier and a medical center in the USA.<sup>72</sup> In the long term, telesurgery could also be used in the longlasting, manned space missions of the future.

Before these goals become a reality, however, several issues must be addressed. Telemedicine of any kind is dependent on continuous and high-quality signal transmission.<sup>59</sup> Although local setup does not theoretically require a surgeon, experienced surgeons must be on hand at the patient's location, ready to take over the operation in case of system or transmission failure. Additionally, because of the necessary technical assistance in both locations, coordination of such efforts, especially across several time zones, has proved challenging.

Another source of difficulty is the fact that medical technology currently is advancing too rapidly for legislation to keep pace. Among the issues requiring attention are interstate and international licensure regulations, billing,



**Figure 55.4** Remote controlled instrumentation and Munich operating room in telesurgery case.

informed consent, and malpractice insurance. It may be necessary to institute committees to set international standards, rules, regulations, and safety measures for the protection of the patient. The stringent technical requirements and costs of telesurgery are currently satisfied only by specialized centers throughout the world. However, the field is expected to expand in the future through wider distribution of robotic systems, and as reliable low-cost communication systems become more readily available.

### **Training devices for minimally invasive techniques**

As mentioned earlier, there is currently a worldwide demand for laparoscopic specialists in many fields of surgery. Since an insufficient number of qualified training programs exists, surgeons currently attend training courses or observe procedures at specialized centers. While initial direct experiences with experts are very important, a constant exposure to the experience of laparoscopic manipulation is mandatory to keep and expand the acquired skills.<sup>63</sup> In a comparison of surgeons who attended a laparoscopic course, See et al<sup>73</sup> found the complication rate for surgeons who did not continually perform minimally invasive procedures three times greater than that of their course colleagues who did.<sup>73,74</sup> It is therefore crucial not only to train qualified laparoscopic surgeons in certified programs but also to ensure ongoing practice and mentoring.

Laparoscopy can be efficiently taught and tested using robotic devices, allowing instruments to be manipulated while various techniques and difficult situations are simulated. With these tools, tutoring by experienced minimally invasive surgeons as well as self- or computer-guided, hands-on training can be performed in a stress-free environment.

A 3-step laparoscopy training system is near completion in our URobotics Laboratory.<sup>18</sup> The first of these devices allows the trainee to become accustomed to the inverted manipulation of laparoscopic tools under direct (3D) vision. Using this system, the trainee inserts instruments through ball-joint trocar ports and operates on phantom or animal specimens. The Step 2 trainer is a closed box with similar entry ports for training under 2D visualization. The Step 3 trainer, presently in the experimental stages, replaces the opaque box used in the Step 2 trainer with a high-fidelity synthetic torso (Figure 55.5) which follows the male anatomy of the Visual Human Project of the National Library of Medicine (NLM). This Step 3 trainer closely simulates true human laparoscopy and reduces the need for surgical training on animals. The torso allows for the in-situ inclusion of abdominal animal organs, presents a disposable abdominal wall that can be



**Figure 55.5** High-fidelity synthetic torso for urologic laparoscopy training. (Courtesy of Johns Hopkins URobotics Laboratory, Johns Hopkins Medical Institutions (JHMI).)

pressurized, and also includes respiratory simulation by connecting the torso to a respirator.

The ideal laparoscopy training method would be virtual reality (VR) based. In surgery, VR trainers provide the opportunity to learn through interacting with a simulated 3D environment. The VR student can perform in many different scenarios and create diverse teaching modules.<sup>75</sup> VR training can provide performance feedback and, perhaps someday, provide certification standards for training urologists.<sup>76,77</sup>

A VR flexible ureteroscopy simulator (HT Medical, Inc., Rockville, Maryland) allows surgeons to practice navigating through, and evaluating, the urinary collection system. Perhaps the most advanced VR simulators in urology thus far have been created by Dr Manyak's research group at George Washington University. The GWU team uses the Visible Human dataset for generating surface-based geometric data. Their systems are specialized VR trainers that provide a realistic experience of the lower urinary tract in endoscopic procedures.<sup>78</sup> The group has developed and continues to expand a computer-based surgical simulator that incorporates a surgical tool interface with anatomic detail and haptic feedback.

The use of VR in training has demonstrated that more experienced laparoscopic surgeons perform surgical tasks with greater accuracy and efficiency than less-experienced surgeons.<sup>79</sup> Improvements in collision detection and graphics, among other things, are presently being tested. Clearly, the widespread distribution of realistic training devices has the potential to improve the skill of laparoscopic urologists worldwide.

## Conclusion

New tools such as surgical robots provide diverse and promising possibilities for improving existing surgical techniques and for developing new ones. Among many other advantages, robots are often able to improve the dexterity and precision with which minimally invasive surgery is carried out.

Several surgical robotic systems have been developed, tested, and cleared by the FDA. Some of these have already demonstrated powerful clinical utility within urology. With continued technological improvements and the emphasis of both sides on strong partnerships between doctors and engineers, surgical robotics will continue to broaden horizons in the practice of urology.

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## Disclosure

Under a licensing agreement between Image Guide and the Johns Hopkins University, Dr Stoianovici and Dr Kavoussi are entitled to a share of royalty received by the University on sales of some products described in this chapter. Dr Stoianovici, Dr Kavoussi, and the University own Image Guide stock, which is subject to certain restrictions under University policy. The terms of this arrangement are being managed by the Johns Hopkins University in accordance with its conflict of interest policies.

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**Part III**  
Minimally invasive  
approaches to pediatric  
urology

## Pediatric laparoscopic renal biopsy: techniques and indication

Paolo Caione and Salvatore Micali

### Indications for renal biopsy

The indications for renal biopsy vary according to the ethnic and age characteristics of population studies and geographical location, since these factors influence the incidence of various renal diseases.

Evaluation of a renal biopsy specimen may be useful in establishing the diagnosis, evaluating the acuteness and severity of the disease process, and determining the degree of reversibility. Clinical and laboratory evidence of glomerulonephropathy, either primary or secondary to systemic disease, is one of the most common indications for examination of renal tissue. Biopsies are done to define the prognosis based on the histologic diagnosis in children with nephrotic syndrome, to establish a diagnosis in children with chronic glomerulonephritis, and to determine the nature of disease and the degree of renal injury in patients presenting clinically with acute glomerulonephritis, particularly when it is severe. Percutaneous renal biopsies are often performed by nephrologists for the assessment of pediatric patients with unexplained azotemia, protein—uria, hematuria, or idiopathic nephrotic syndrome resistant to steroids.<sup>1</sup> Moreover, acute nephritis, acute renal failure, chronic renal insufficiency, systemic diseases, and follow-up of disease could be considered clinical indications for renal biopsy. In patients with systemic disorders such as lupus erythematosus or Henoch-Schonlein syndrome, examination of renal tissue may be necessary to document involvement of the kidney and to provide information concerning the histologic diagnosis and magnitude of the renal injury. Hypertension without other signs of renal involvement is not an indication for renal biopsy in children. The rate of serious complication of biopsy is increased in hypertensive individuals. If renal disease is suspected as the etiology of the hypertension and if a biopsy is to be performed, the hypertension must be well controlled prior to the procedure. Prompt interpretation of biopsy tissue from renal allografts apparently undergoing acute rejection may aid in determining the correct therapy. Biopsy may play a critical role also in the diagnosis of recurrent disease in renal transplants and in determining the presence or absence of cyclosporine toxicity. The use of fine-needle biopsies has been advocated for the latter purpose.

Most authors agree that renal biopsy is of little value in the assessment of children with urinary tract infection. It has been applied only occasionally in the evaluation of cystic and dysplastic disorders. It is relatively contraindicated when the presence of an

intrarenal neoplasm is suspected because the procedure may lead to intra-abdominal dissemination of the tumor.

Percutaneous needle renal biopsy is the current standard approach, usually performed under ultrasound control. Ultrasonography and radioisotopic scanning could precede biopsy in an attempt to differentiate acute from chronic renal failure and to exclude extrarenal or urologic lesions such as obstruction. Over time, the contraindications of percutaneous needle biopsy of the kidney have decreased with the advent of reliable, minimally invasive imaging techniques and the development of adequate protocols for patient monitoring during the early post-biopsy period.<sup>2</sup> The development of small-caliber biopsy needles has also contributed to the increased safety and reduced morbidity of this technique.

With improvements in safety and reliability, several clinical conditions that were recently considered absolute contraindications for percutaneous biopsy, i.e. solitary kidney and obesity, are now considered relative contraindications.<sup>3</sup> However, there are some pediatric patients in whom a percutaneous approach may be risky, the only remaining option being a renal biopsy under direct visualization. Currently, relative indications for renal biopsy under direct visualization are age less than 7 years old, uncontrolled hypertension, bleeding disorders, and anticoagulant medications.

### **Technical options for renal biopsy**

#### *Percutaneous needle biopsy*

The patient can be treated as an outpatient. Ultrasound examination is performed to confirm the normal position of the kidney without anatomical anomalies. Laboratory evaluation must include a complete blood cell count with normal platelet count, partial thromboplastin, prothrombin time, fibrinogen level and bleeding time. The biopsy is timed so that an experienced technician or pathologist can attend, to ensure prompt processing of the biopsy tissue.

Food and drink should be withheld for at least 6 hours before biopsy. The child should be sedated, but awake, so if possible he can cooperate during the procedure. The patient lies in the prone position with a rolled sheet under the abdomen and draped in a sterile fashion. The left kidney is usually preferred, but either side can be chosen for biopsy. Then, the lower pole of the kidney is marked on the skin with a pen after localization by ultrasound. Local anesthetic is infiltrated first in the skin, and then in deeper tissues, taking care not to enter the kidney. A small incision is made through the skin. A disposable core tissue biopsy needle (16-gauge) mounted on a biopsy gun (Bard Magnum, CR Bard, Inc., Covington, Georgia) is preferred for biopsy in larger children (over 5 years old) because of its ease of use and sharp cutting edge. The biopsy needle can now be inserted into the desired position. When the kidney capsule is punctured, a loss of resistance can be felt. The needle will move with inspiration when the child is asked to breathe, confirming that it is within the renal parenchyma. The entire needle with tissue sample is then removed. Usually, two cores of tissue are necessary for optimal evaluation. If tissue cannot be obtained after several passes, the biopsy should be attempted another way. The child is kept supine in bed for 24 hours, urine is observed for

gross hematuria and the hematocrit should be rechecked at 4 and 24 hours after the biopsy. The child may be discharged the next day if no complications arise.

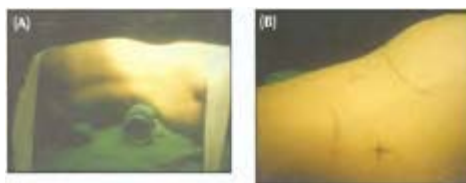
### *Retroperitoneoscopic renal biopsy*

Following the administration of adequate general endotracheal anesthesia, a transurethral Foley catheter and a nasogastric tube are placed. The patient is placed in the full flank position and secured to the operating table (Figure 56.1). A two-port technique is used via a retroperitoneal route: a 10 mm laparoscopic port is placed between the iliac crest and the 12th rib, in the posterior axillary line. A 5 mm port is inserted at the same level on the anterior axillary line (Figure 56.2). In all children the first trocar is positioned under direct vision using the Visiport (AutoSuture, US Surgical Corporation, Norwalk, Connecticut). This device allows the surgeon to incise and advance the cannula through each tissue layer under direct vision until the retroperitoneal space is reached. Insufflation with CO<sub>2</sub> at 15 mmHg is started. The laparoscope is then used to bluntly dissect the retroperitoneal space and mobilize the lateral peritoneum from the anterior abdominal wall (Figure 56.3). The 5 mm port is also inserted under direct vision (Figure 56.4). Finally, the CO<sub>2</sub> insufflation pressure is turned down to 8–10 mmHg. Minimal dissection is required in order to expose the lower pole of the kidney (Figure 56.5). Short 5 mm laparoscopic cut biopsy forceps are used to grasp two superficial cortical biopsy specimens (Figures 56.6 and 56.7). The biopsy site is fulgurated with monopolar or bipolar electrocautery, and a sheet of oxidized cellulose (Surgicel, Johnson & Johnson, Arlington, Texas) is applied. Upon conclusion, the gas is evacuated and the skin is closed with absorbable sutures. Time required is usually 20–40 min. Blood loss tends to be minimal. The retroperitoneoscopic procedure may be performed on an outpatient basis or the patient may spend the night in hospital. Patients are allowed to return to their usual activities within a few days.

### *Traditional open renal biopsy*

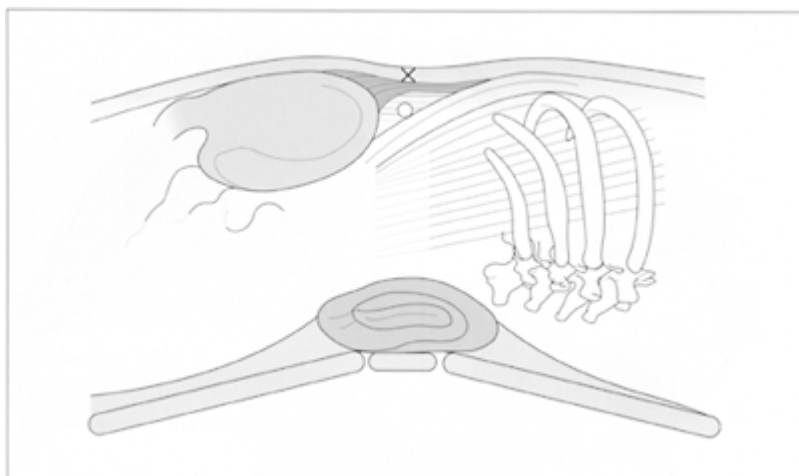
This technique today is rarely used because minimally invasive techniques are preferred in almost all the pediatric hospitals, either with percutaneous needle or laparoscopic procedures.

Open biopsy is performed under general anesthesia. The kidney can be directly visualized even through a small muscle-splitting lumbotomy incision. One advantage of the open approach is that a larger sample may be obtained via wedge biopsy than can be obtained with the laparoscopic biopsy forceps.



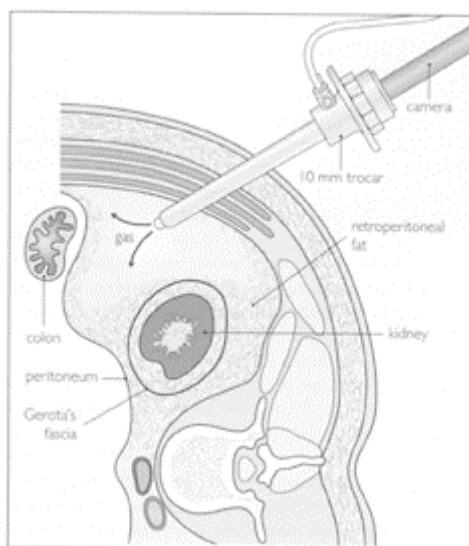
**Figure 56.1**

(A) Patient position for retroperitoneal open renal biopsy or laparoscopic biopsy. (B) Trocar positions are underlined.



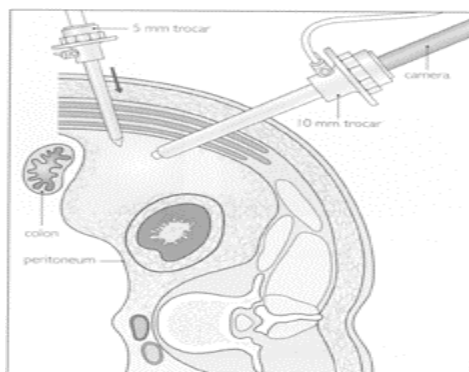
**Figure 56.2**

Anatomic landmarks for retroperitoneal laparoscopy: 12th rib, iliac crest. Trocar positioning for minor renal operative procedures through retroperitoneal laparoscopic access: X=10 mm port, O=5 mm port.



**Figure 56.3**

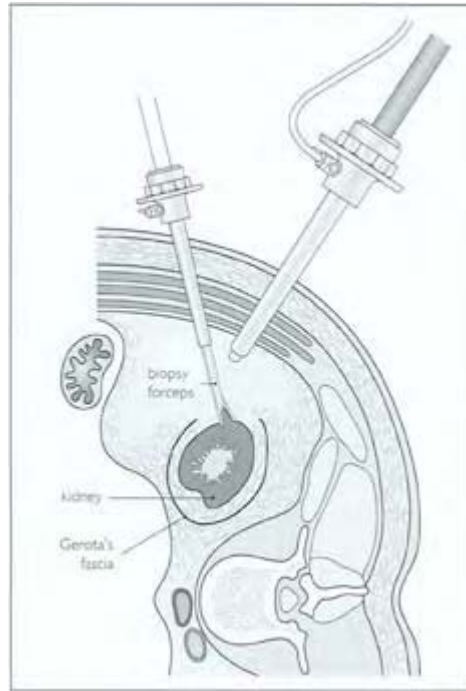
After retroperitoneal access is obtained, blunt dissection is used to mobilize the lateral peritoneum from the anterior abdominal wall.



**Figure 56.4**

After the development of the retroperitoneal space, a 5 mm trocar is placed at the anterior axillary line.

Care must be taken to prevent entry into the peritoneal cavity.



**Figure 56.5**

After localization of the kidney, Gerota's fascia is incised and the renal parenchyma is exposed.



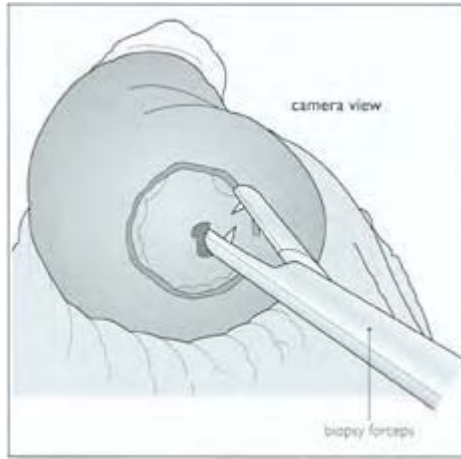
**Figure 56.6**

Pediatric biopsy forceps (A) and particular of the jaws for renal biopsy (B).



### Clinical considerations, complications, and results

Histologic evaluation of renal tissue is often necessary in the evaluation and management of several renal diseases. Pathologic diagnosis often provides useful information in determining prognosis and guiding treatment.<sup>1,4,5</sup> Several methods to sample renal tissue are available, including



**Figure 56.7**

Renal core biopsies are obtained via a 5 mm laparoscopic cut biopsy forceps.

blind and image-guided percutaneous needle biopsy or aspiration and open or laparoscopic approaches. Percutaneous needle biopsy is the most common method of sampling renal tissue in adults and pediatric patients, because it is minimally invasive and can be performed under local anesthesia with minimal morbidity.<sup>3</sup> Unfortunately, as many as 5–20% of percutaneous needle biopsies yield inadequate renal tissue for diagnosis<sup>6</sup> and significant complications such as hemorrhage and even renal loss have been reported.<sup>7–9</sup> Moreover, in children younger than 7 years of age who do not cooperate adequately during the procedure, the percutaneous approach may be hazardous even under local anesthesia.

In addition, our experience in children indicates contraindications to percutaneous renal biopsy, such as uncontrolled hypertension, bleeding disorders, anatomic abnormalities, solitary kidney, and anticoagulant medication.<sup>1,7,10</sup> In these patients, a renal biopsy under direct vision may be preferred (Table 56.1).

The development of laparoscopic renal biopsy now provides a minimally invasive alternative to open renal biopsy. General anesthesia is required as in the open technique, but the kidney is better identified with the optical magnification of the laparoscopic lens. Only two ports are required for the retroperitoneal procedure. During our retroperitoneoscopic procedure, a nephrologist is present in the operating room, and a

preliminary macroscopic examination of the kidney, including site, size, color, and bleeding intensity is performed. Moreover, biopsy and hemostasis are achieved under direct vision in a controlled minimally invasive fashion.<sup>11-14</sup>

**Table 56.1** *Indications for pursuing a laparoscopic approach in 20 consecutive patients*<sup>19</sup>

| Patient No. | Age (years old) | Contraindications for percutaneous biopsy |
|-------------|-----------------|---|
| 1           |                 | 10 Uncontrolled hypertension              |
| 2           |                 | 4 Uncontrolled hypertension, age          |
| 3           |                 | 4 Age                                     |
| 4           |                 | 7 Age, parents' request                   |
| 5           |                 | 7 Age                                     |
| 6           |                 | 4 Uncontrolled hypertension, age          |
| 7           |                 | 11 Uncontrolled hypertension              |
| 8           |                 | 17 Anticlotting medications               |
| 9           |                 | 14 Uncontrolled hypertension              |
| 10          |                 | 2 Age                                     |
| 11          |                 | 16 Uncontrolled hypertension              |
| 12          |                 | 11 Medullary cystic disease               |
| 13          |                 | 12 Uncooperative patient                  |
| 14          |                 | 5 Age                                     |
| 15          |                 | 11 Parents' request                       |
| 16          |                 | 9 Unsuccessful previous needle biopsy     |
| 17          |                 | 14 Uncontrolled hypertension              |
| 18          |                 | 18 Parents request                        |
| 19          |                 | 4 Age                                     |
| 20          |                 | 5 Age                                     |

Using an entirely retroperitoneal approach, we were able to obtain sufficient renal tissue for the histopathologic diagnosis in 20 children (Table 56.2). No bleeding complications or hematuria occurred in any of our patients, and none of them required blood transfusion. The high success rate and lack of bleeding complications in our experience is equal to that reported in large open renal biopsy series.<sup>6,15,16</sup> In contrast, the incidence of bleeding complications was found to be 5.0% in a contemporary percutaneous renal biopsy series.<sup>9</sup> We feel that our technique potentially reduces the risk of hemorrhage, hematuria, and the development of secondary arteriovenous fistulas as compared with the percutaneous needle approach. Two primary advantages are noted: hemostasis is achieved and confirmed under direct vision and the cup biopsy forceps yields generous and superficial cortical specimens, without injuring the underlying central vessels or the collecting system. Biopsy needles,

**Table 56.2** *Hystopathologic diagnosis in the 20 retroperitoneal laparoscopic renal biopsies<sup>19</sup>*

| Patient No. | Age (years old) | Pathologic diagnosis  |
|-------------|-----------------|---|
| 1           | 10              | Proliferative glomerulonephritis, Henoch-Schönlein syndrome |
| 2           | 4               | Proliferative glomerulonephritis                            |
| 3           | 4               | Proliferative glomerulonephritis                            |
| 4           | 7               | Alport's syndrome   |
| 5           | 7               | Proliferative glomerulonephritis                            |
| 6           | 4               | Thrombotic microangiopathy                                  |
| 7           | 11              | Proliferative glomerulonephritis                            |
| 8           | 17              | Proliferative lupus glomerulonephritis                      |
| 9           | 14              | Proliferative lupus glomerulonephritis                      |
| 10          | 2               | Proliferative glomerulonephritis, Henoch-Schonlein syndrome |
| 11          | 16              | Proliferative glomerulonephritis                            |
| 12          | 11              | Medullary cystic disease                                    |
| 13          | 12              | IgA nephropathy   |
| 14          | 5               | Alport's syndrome   |
| 15          | 11              | Alport's syndrome   |
| 16          | 9               | IgA nephropathy   |
| 17          | 14              | Mesangial proliferative glomerulonephritis                  |
| 18          | 18              | IgA nephropathy   |
| 19          | 4               | Focal segmental glomerulosclerosis                          |
| 20          | 5               | Henoch-Schonlein syndrome                                   |

which can potentially reach collecting system and/or large segmental vessels, are avoided.

Squadrito and Coletta<sup>17</sup> were the first to report laparoscopic renal biopsy in a human patient via a transperitoneal approach. Gaur<sup>18</sup> popularized the retroperitoneoscopic approach and reported the use of a balloon to develop the retroperitoneal space. Gaur et al.<sup>11</sup> first reported a series of 17 patients in whom retroperitoneoscopic renal biopsy was performed. The authors reported two complications in their series. When deep cup biopsies were performed, hemostasis was achieved through an enlarged incision in one case. Another patient developed gross hematuria, which resolved spontaneously in 2 days. We prefer the retroperitoneal approach for renal biopsy because there is less risk of injuring intraperitoneal viscera or causing a postoperative ileus.<sup>19</sup> According to our experiences, we have modified the Gaur technique by entering the retroperitoneum using the Visiport device through a standard 1 cm incision, rather than performing a larger cutdown. We rapidly develop the retroperitoneal space with a blunt technique, using the laparoscope rather than a balloon.<sup>20</sup> We find that the retroperitoneal space in children is smaller than in adults, and the peritoneum is thin and easily entered. Therefore, the Visiport device enables us to see the peritoneum and preserve its integrity safely. In addition, our technique uses only two ports as compared to the three commonly required for other techniques.

In small children we recommend the use of short pediatric instruments (dolphin forceps, scissors, and biopsy forceps). At the end of the procedure, the insufflation

pressure is gradually decreased, and the biopsy site is observed and any bleeding is controlled.<sup>21</sup>

### Conclusion

Laparoscopic renal biopsy is a safe, reliable, and minimally invasive alternative to open renal biopsy. With experience and a systematic, anatomic approach, retroperitoneoscopic renal biopsy can be efficiently performed in pediatric patients older than 6 months of age.

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## Minimally invasive approaches to the ureteropelvic junction and upper ureter

Craig A Peters

### Pathologic anatomy of the ureter

The basis for nearly all pathologic conditions of the ureter in children is abnormal ureteral development, which follows fairly consistent patterns. The ureteral pathology itself is rarely the problem, but the effects on urinary transit and renal function are the principal concerns. Understanding the patterns of abnormal ureteral development is essential to selection and application of appropriate therapeutic interventions.

### *Embryology*

The ureter develops in conjunction with the kidney in a mutually inductive process. Recent evidence has suggested that the metanephric blastema, the precursor for the ultimate kidney, may actively induce ureteral budding,<sup>1</sup> in contrast to separate ureteral budding with subsequent induction of the metanephric mesenchyme by the ureteral bud. This would suggest that any renal mesenchyme abnormalities might then induce ureteral budding anomalies, such as reflux or ectopia. There is clearly an association between the two, and this was best described by the Mackie-Stephens theory: progressively more anomalous and ectopic ureteral budding leads to increasing degrees of renal dysplasia. While this theory has provided an explanation for many patterns of anomalous development, it does not explain all, and exceptions can be found. It does not permit a simplistic approach to these anomalies either, and their features must be carefully evaluated to develop an appropriate treatment plan for each child.

The molecular signals mediating ureterorenal development are now being elucidated and include a variety of signaling molecules (Pax2),<sup>2</sup> Foxc (transcription factor),<sup>1</sup> Wnt-6,<sup>3</sup> Tmp21-I (a protein traffic regulator),<sup>4</sup> Vitamin A (with Ret, a signaling molecule),<sup>5</sup> glial-derived neurotrophic factor (GDNF),<sup>2</sup> endostatin (an angiogenesis inhibitor),<sup>6</sup> matrix metalloproteinases,<sup>7</sup> and components of the angiotensin system.<sup>8</sup> The regulation of branching morphogenesis is a critical element in normal ureterorenal embryogenesis and has been the subject of much investigation relevant to normal ureteral development.<sup>9,10</sup> Several excellent reviews of the current focus of research on ureterorenal development have been published.<sup>11-13</sup>

During ureteral development there is good evidence that the ureter passes through a stage in which the initially tubular structure condenses into a solid cord.<sup>14</sup> This feature of development has been highly quoted and the evidence is fairly strong. It is observed in both human and is that many obstructive conditions are considered due to animal

embryonic specimens. The importance of this stage incomplete subsequent recanalization. The specific causes for this are unknown, as is the process of recanalization. Presumably it is mediated by increased growth of the peripheral aspects of the ureter. This may relate to the process of muscular ingrowth into the ureter from the surrounding mesenchyme.<sup>15</sup> The driving factors in these processes are still undefined, but their elucidation may provide useful insight into pathological processes.

Development of the ureteropelvic junction (UPJ) itself, the site of the vast majority of ureteral obstructions is relatively undefined.

The response of the ureter to anomalous development is important to consider as well, since it may determine the efficacy of various treatment modalities. Obstruction and reflux are the most common patterns of pathology for the ureter and each induces similar, but likely, functionally distinct responses. These responses are probably very similar to those of the renal pelvis as well. In general, any process that induces dilation of the ureter is characterized by increased amounts of ureteral smooth muscle with increased interstitial connective tissue.<sup>16</sup> The underlying mechanisms of these pathologic responses, which may be compensatory, but nonetheless pathologic, are being investigated. There seem to be increased expression of smooth muscle, suggesting dysregulation of ureteral smooth muscle cell (SMC) growth factors.<sup>17</sup> Increased extracellular matrix (ECM) may be the product of altered balance between connective tissue synthesis and breakdown.<sup>18</sup> Breakdown may itself be the product of imbalance between degradation and natural inhibition of degradation. These processes are seen in the bladder as well. Recognizing the patterns of these processes and their driving forces may permit more specific therapy for the abnormal ureter. It is also important to recognize that treatments directed at the ureter are dealing with abnormal tissue that may be fibrotic and poorly compliant. This will clearly affect healing and remodeling, and may well explain some failures of therapy. Precise definition of those aspects, however, is still lacking.

As the ureter develops, it is involved in a delicate two-way dance with the developing kidney and their respective fates are intertwined. Mutual coinduction is probably the most appropriate description of this process. Clearly, then, the abnormal ureter may be associated with an abnormal kidney. This is not, however, certain, and detailed evaluation is still needed. It should also not be assumed that abnormalities of kidney function associated with an abnormal ureter are immutable and fixed. This is particularly true in the setting of apparent obstruction, in which the abnormal ureter, with deranged function, may cause worsening of renal function that may already be less than normal.

### *Pathologic patterns*

The most common abnormality of the ureter is ureteropelvic junction obstruction (UPJO). Because this is a spectrum of disorders, precise definition of the incidence is difficult to establish. In prenatal detection, the incidence is between 0.1 and 2.0% of cases, depending upon the threshold for 'hydronephrosis'. Thomas reports in-utero dilation to have an incidence of 1 in 60 pregnancies with 1 in 500 having a significant urologic problem, half of which were UPJ abnormalities.<sup>19</sup> There is a male predominance (2:1) of these conditions, which also occur more often on the left side (2:1). The clinical and functional significance of any given UPJO is very controversial. Prenatal ultrasound has shown many patients with an apparent UPJO that may resolve spontaneously, challenging

the accuracy of other series. The controversy of the functional significance of any of these conditions remains unsettled. Treatment options must therefore be viewed in the context that no gold standard exists for defining a 'significant' or 'surgical' UPJO. Within the group of UPJOs are those crossed by a lower pole renal vessel, usually an artery, which produces a mechanical fixation point of the ureter, about which it will kink. This may produce intermittent obstruction, with attendant acute symptoms, so-called Dietl's crisis.<sup>20</sup>

### Pathophysiology of ureteral anomalies

The most significant ureteral anomalies produce obstruction, and the response of the developing or juvenile kidney is the key deleterious effect. The spectrum of severity in ureteral obstruction is paralleled by the spectrum of response of the kidney. Precise detection of where in the spectrum a particular patient's condition may fall remains an ongoing challenge and is controversial. This is particularly true of patients whose obstruction has been detected by prenatal ultrasound and who are usually symptom-free. It is clear that some UPJOs produce an ongoing loss of renal function, with the further risk of infection, pain, or stone formation. Others, however, and a large number, are less severe and appear to resolve spontaneously when followed nonsurgically. Distinguishing the two may be difficult, and there is a broad gray area in which the distinction is unclear. The response of the prenatal kidney is complex, yet viewed broadly it reflects the altered growth and differentiation of various components of renal function.<sup>21</sup> There are injury responses such as fibrosis that are also important and play a significant role in the functional response to obstruction. These responses should ultimately permit more accurate determination of the severity of the obstruction from a renal standpoint and allow clinical decisions that reflect more than simple appearance. The functional effects at the ureteral level are still important and are clearly the foundation of the renal response.

The function of the ureter is to transmit urine from the kidney to the bladder at low pressure, and be able to do this efficiently at differing rates of urine production. This is mediated through a peristaltic action of the ureter in which a regular progression of smooth muscle contractions and relaxations travels from the calyces through the renal pelvis to the ureter. These form discrete boluses of urine, which are trapped by the contracting ureter above and propel the urine downward. Disturbances in this mechanism result from three sources.

**1. Mechanical obstructive effect such that the rate of urine passage at the pressure generated from above is much lower than the urine output.** While the ureter may still be patent, it is limited in its volume capacity. To some extent, this effect can be overcome by increased pressure, but clearly this can be limited and may have negative hydrostatic effects on the kidney. Of course, this is what will ultimately lead to the indication of obstruction, hydronephrosis, as the system attempts to maintain normal function in the face of reduced volume capacity. Above the point of hold-up, several things may happen and these include the second cause of disturbed urine transmission.

**2. With increasing pressures, the system tends to dilate and this reduces wall tension according to Laplace's law.** This will serve, presumably to protect the tissues



from pathologic tension/pressure, particularly the renal parenchyma, but in so doing, it will reduce the ability to transmit the peristaltic wave. This is due to the inability to coapt or come together with the peristaltic wave. This, then, permits regurgitation of urine backward, much the same as in valvular regurgitation of the heart. As the dilation progresses, transport efficiency declines and the system is in a decompensated mode.

**3. The third means by which urine transport is impaired in the ureter is by way of disordered ureteral peristalsis.** This results in lack of propagation or disordinated propagation of the peristaltic wave. It is presumed that developmental anomalies of the ureter can lead to segmental maldevelopment, where the contraction wave is not conducted appropriately. Histologic examinations of resected UPJ segments show various patterns of disordered smooth muscle organization, increased connective tissue, and narrowing.<sup>22–26</sup> These areas may not be able to propagate the ureteral contraction appropriately. Similarly, surgical division of the ureter can also be seen to disrupt propagation, but this can heal.<sup>27–29</sup> Persistent apparent obstruction following surgery may be explained by failure to re-establish appropriate cell-to-cell interactions that seem to be the basis for peristaltic propagation.

Disordered urine transport has been used as the basis for several diagnostic studies of ureteral pathology, including the pressure perfusion test (Whitaker test) and the MAG3 diuretic renogram. Interpretation of the results of these tests remains controversial. Clearly, a better understanding of how the ureter fails to transmit urine in pathologic states, as well as the effect of that failure on renal function, are the keys to diagnosing significant obstruction and may yield insights into more specific therapies.

### *Ureteral healing*

Ureteral healing is an important aspect to be considered in treatment modalities, and our understanding is approaching the point where we may be able to enhance healing and identify patients at risk for complications of healing. Early studies of the ureter have indicated that smooth muscle regrowth is rapid and occurs from the outside inward.<sup>28,29</sup> This allows circumferential reconstitution of the ureter within days and subsequent muscularization shortly thereafter. This experimental observation supports the empiric observation that was the basis for the Davis intubated ureterotomy, in which a narrow ureter could be longitudinally incised, stented, and would regenerate the ureteral wall and demonstrate appropriate peristalsis with healing. This is the basis for modern endopyelotomy. Dismembering the ureter was initially considered to be doomed to failure, due to interruption of peristaltic transmission. Experimental studies in the 1950s showed that peristalsis would regenerate within 4 weeks, indicating reconstitution of the cell-cell junctions transmitting the peristaltic wave.<sup>30</sup> These processes do not always succeed and there is still more to be learned about ureteral healing. Several model systems have been developed and may provide insight into the healing of the ureter and ways in which it may be enhanced.<sup>31,32</sup>

## Clinical presentation and evaluation of ureteral anomalies

### *Ureteropelvic junction obstruction*

The classic presentation of UPJO is episodic flank pain with nausea and vomiting, often triggered by a fluid load. This pattern may be readily mistaken for gastrointestinal conditions and many patients have undergone unrevealing gastrointestinal investigations until a dilated kidney is noted by chance. The pattern of intermittent severe pain that totally resolves and often occurs at night should at least initiate a cursory consideration for renal pathology using ultrasound. Occasionally, this will be normal when no symptoms are present, and if the pattern is suggestive, those patients are best approached by obtaining an emergency ultrasound during an attack of colic. While this may be cumbersome, it may be the only way to confirm the diagnosis. In some of these cases, stimulating a high urine output with diuretic will trigger an attack. This can be done with furosemide and ultrasound or with a diuretic renogram. Occasionally, a crossing lower pole vessel may be identified sonographically, but this is difficult and not a universal ultrasonic finding.

Currently, the most common pediatric presentation of UPJO is through prenatal detection of hydronephrosis. This group of patients poses the greatest challenge, as they are generally asymptomatic and present with a wide spectrum of severity. Significant controversy has evolved in the last 15 years as to which patients need to undergo any corrective intervention, and the concern for selecting patients in whom the apparent obstruction is severe enough to risk affecting renal function and who will not resolve spontaneously has become a major challenge.<sup>33,34</sup> This chapter cannot hope to cover or resolve this controversy, but the basic approach to these patients can be presented in the context of choosing therapy using minimally invasive techniques. Of course, as those minimally invasive techniques evolve, the therapeutic balance between the risk and impact of intervention and observation will also change, and may facilitate decision making.

In children with prenatally detected hydronephrosis, the initial level of decision-making is to decide who should have testing. This remains to be definitively defined, as it depends largely upon the level of certainty that one desires and the level of risk reduction sought: it is difficult, if not impossible, to quantitate and generalize. For practical purposes, functional testing beyond ultrasonography is recommended for those with some likelihood of requiring surgical intervention. These are the patients with generalized caliectasis of the affected kidney. A diuretic renogram is then recommended to assess both relative function by uptake and drainage of the affected kidney. The interpretation of these data remain controversial, but in the setting of a kidney with normal uptake and drainage that is not markedly abnormal, observational management is reasonable.<sup>35</sup> The thresholds for intervention are fluid, and largely dependent upon the individual's as well as the parents' level of comfort. Intravenous pyelography (IVP) is an option if there is question about the anatomic basis for obstruction or if there is discordance between the ultrasound and radio-nuclide images. Many of these patients may be followed expectantly, although the burden of follow-up must be communicated to the parents. The

decision as to how long to monitor these patients when the hydronephrosis does not resolve is difficult.

### *Ureteral polyps*

A rare etiology of apparent UPJO is a ureteral polyp(s) at the UPJ.<sup>36,37</sup> These are considered to be both congenital and acquired, and their pathogenesis is poorly defined. They may be intermittent in their obstruction, or produce a constant degree of obstruction, leading to hydronephrosis. They are not usually visualized on ultrasound but may be seen on retrograde pyelography or IVP. Surgical management is not different from conventional UPJO and the affected segment, which should contain the pedicle of the polyp, is resected and a spatulated anastomosis performed. Endoscopic resection is a reported option, limited only by ureteral size.<sup>38</sup> Histologically, these polyps show a transitional cell surface and an edematous core with a vascular stalk. They may be multilobulated. No difference in postoperative follow-up is needed.

### *Megaureter (obstructive)*

Recognition of the obstructed megaureter is the essential part of therapy. The dilated ureter may be missed on ultrasound imaging. The best image to exclude a dilated ureter is the bladder view, in which the dilated distal ureter is usually noted. Determining if the ureterovesical junction obstruction (UVJO) is functionally significant is more difficult, as many will resolve spontaneously.<sup>39</sup> Those presenting with symptoms in later life are more likely to benefit from intervention. Prenatally detected UVJO rarely undergoes surgical intervention today, but those with extreme dilation and reduced function are likely to benefit from surgical therapy.

## **Goals of therapy and clinical decision making**

It should always be kept in mind that the goal of therapy of the dilated renal pelvis is to protect renal function and reduce the risk of complications due to stasis. The judgment as to which patient is at what level of risk for functional loss or complications is fraught with uncertainty, and remains controversial. While it may not be settled in this review, the basic principle to be followed might be that if renal function is already impaired, it is at higher risk to continue to do so, and that if a process has not improved in a reasonable waiting period (e.g. 2 years) it might be unlikely to do so. If the degree of dilation is of a similar nature as those associated with decreased function (severe by whatever scale), even if function is preserved, intervention seems reasonable.

If early surgery is not deemed to be appropriate, a monitoring program needs to be adopted to prevent unrecognized functional decline. The specifics of this are also poorly defined. Annual or every 2-year functional studies would seem a minimum of security. All of this is predicated on the notion that if functional decline is noted, intervention at the time of detection will permit return to prior function. This is not the universal experience in observational studies and some recognition of this risk is essential.<sup>34,40</sup>

In those patients in whom surgical repair is deemed appropriate, the options available should be discussed with the family in a realistic context. In part, this is age-dependent in that some of the minimally invasive procedures have little track record in infants. None have the degree of certainty of open surgical repair, which remains the gold standard of therapy, but there is ongoing development of less-invasive modalities.

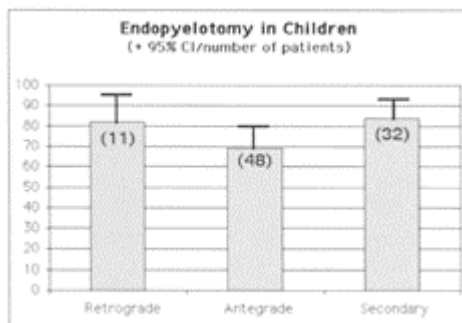
## Ureteropelvic junction obstruction

### *Endopyelotomy*

#### **Antegrade direct vision**

Endopyelotomy in children may be performed using an antegrade or retrograde approach, and in smaller children the antegrade technique is the most reasonable. There are several reports of this method in primary UPJO,<sup>41-43</sup> and the original reports were related to secondary obstructions.<sup>44</sup> In the dilated pelvis, access is not difficult, although it is important to access from the mid pole of the kidney rather than the lower pole to facilitate direct access to the UPJ. A guide wire is passed down the ureter, which may be difficult, but this is essential, as stenting after the incision is necessary. Incision may be performed using either a hot or cold knife. With small numbers in each category the potential success rate is about 82% ( $n=11$ ) for retrograde, 69% ( $n=48$ ) for antegrade, and 84% ( $n=32$ ) for secondary endopyelotomy in pediatric series (Figure 57.1) This compares to a general average of about 80–85% success in adult series. Risk factors identified for failure include the presence of a crossing vessel, as indicated by lower success rates in symptomatic patients.<sup>45</sup>

The basic principle of this approach, of course, is based upon the Davis intubated ureterotomy, in which the incised and stented ureter will tubularize itself, including musculature within several weeks, and regain peristaltic function. Today, this concept is well used in the Snodgrass tubularized incised plate hypospadias repair. The critical



**Figure 57.1**

Endopyelotomy in children.

parameters that mediate ureteral healing in this context remain unknown, although a recent study suggested that the cytokine transforming growth factor  $\beta_1$  (TGF- $\beta_1$ ) may play an important role in healing.<sup>46</sup> The importance of developing this understanding would be in the ability to manipulate these healing programs to increase efficacy. The basic principles tell us that to be successful the incision should be complete, through the entire wall of the ureter, which is usually signaled by visualization of retroperitoneal fat.

Duration of stenting usually generates debate and there are no clear data in children undergoing endopyelotomy. A reasonable compromise would be between 2 and 4 weeks.<sup>47</sup> Leaving a stent for 6 weeks is difficult if it is external.

### **Retrograde incision/balloon dilation**

Retrograde endopyelotomy in children is largely limited by the size of the patient. Current technology permits ureteral access in almost any child, but the manipulative instruments are limited. There is no Accusize-type system that could be passed into a child younger than 6 or 8 years old without predilation. No custom-built incising instruments are available to date. Direct vision incision requires access to the proximal ureter and this can be performed, and often is facilitated with prestening. The cold knife instrument is larger than most ureters of children under 6 years old could usually tolerate. Smaller incising systems may be put together, but none of these have any background of use. The Accusize is the most established instrument for this purpose, using complete radiographic control, and yet can realistically be used only in adolescents.<sup>48,49</sup>

### *Balloon rupture*

A limited series of infants with UPJO were presented in whom balloon rupture of the UPJ was presented, suggesting that this might be a viable option for early obstruction.<sup>50,51</sup> This method has not been reported elsewhere and the follow-up period is short. The concept is probably similar to the intubated ureterotomy in that the rupture produces a single line of rupture in the ureter; however, the uncontrolled and traumatic nature of the procedure seems counterintuitive for pediatric use. At present it remains a procedure that is yet to be proven with long-term outcomes studies.

### *Percutaneous pyeloplasty*

A recent report in adults has presented a method combining endopyelotomy and laparoscopic pyeloplasty.<sup>52</sup> This method is based upon percutaneous access and incision of the UPJ. A Heineke-Mikulicz closure of the longitudinal incision is performed to open the narrow UPJ. The closure is performed using a device that permits placement of two or three sutures to allow transverse closure and knot tying that is performed extracorporeally. There are no reports in children as yet, and the bulk of the instruments and lack of precision of suture closure seem at odds with standard pediatric practice, yet the concept is novel and intriguing.

*Laparoscopic pyeloplasty*

Laparoscopic pyeloplasty has been performed and reported in several dozen children and has shown itself to be technically feasible and effective. The precise parameters of its utility and generalizability remain to be defined. With new robotic technology, it may become more readily applied by a wider spectrum of urologic surgeons.

**Dismembered pyeloplasty**

The standard procedure used in lap pyeloplasty is a dismembered method, based upon the Anderson-Hynes approach that is the standard of open surgery. Lap pyeloplasty was first reported in 1993<sup>53,54</sup> and in young children in 1995,<sup>55</sup> yet there have been a limited number of reports since then, in contrast to large numbers in the adult literature.<sup>56-59</sup> Success rates seem to be acceptable and close to or equal to open surgical outcomes, yet the procedure has clearly not taken hold. The success depends upon delicate suturing and this seems to be the limiting feature. Unless one has the chance to perform numerous laparoscopic procedures and to develop the skills of intracorporeal suturing, embarking on a lap pyeloplasty in a child is a challenging undertaking. The reported series that include both transperitoneal and extraperitoneal approaches indicate that the procedure can be effective with steadily improving surgical times and excellent outcomes.<sup>56-59</sup> Hospital stay seems shorter, but this is difficult to ascertain as many of the series are from countries where surgical stay is distinctly different than in the United States. It may be very difficult to prove that this approach is 'better' than open surgery. The impact of the postoperative recovery and the scar is difficult to assess in children. These are difficult parameters to assess in an adult, and even more so in a child. It is also a challenge to know how a family will interpret the impact of a permanent large scar in contrast to small laparoscopic incisions.

In a comparison of open and laparoscopic pyeloplasty,<sup>13</sup> school age and adolescent patients underwent laparoscopic pyeloplasty (mean age 15 years old) and 11 open pyeloplasty (mean age 9 years old). All patients had successful repair of UPJO at greater than 12 months follow-up. Mean perioperative narcotic use was similar between the groups. However, both hospital stay (2.6 days vs. 5.6 days) and operating room time (3.68 hours vs. 4.19 hours) were shorter for laparoscopic vs open pyeloplasty.<sup>59</sup> Although open pyeloplasty times in this range are unlikely to be the norm, the study demonstrates the potential for equivalent outcomes without a burden of increased operative times.

Both transperitoneal and retroperitoneal approaches have been used for lap pyeloplasty in children. The relative merits and challenges of each are shown in Table 57.1. It is intuitively more appealing to approach the kidney from the retroperitoneum, but it is difficult to demonstrate that this is 'better'.<sup>58,62</sup>

Transperitoneal lap pyeloplasty is performed with the patient on the operative table, having a wedge support under the affected side of the patient. The table is tilted to lower this side and allow transperitoneal access of the camera and working instruments. Once these instruments are in place, the table is turned to raise the affected kidney. The pelvis may be readily visible through the peritoneum, in which case a transmesenteric approach may be used. Alternatively, the colon is reflected medially to expose the kidney and

pelvis. The ureter is dissected free of attachments. This is done carefully to avoid devascularizing the ureter. Once the renal pelvis is defined, the UPJ can be identified and a traction suture placed at the most dependent portion of the pelvis. A hitch stitch is often helpful in lifting the renal pelvis, after being passed through the anterior abdominal wall. After ureteral spatulation, the anastomosis is begun at the vertex of the spatulation to the most dependent portion of the renal pelvis. A running monofilament suture is used for the closure, usually 5–0 or 6–0, with the back side being closed first followed by the anterior. Placement of a stent is optional, but for conventional laparoscopic pyeloplasty, it has been our preference. In that case, no drain is used. A more detailed suturing strategy is outlined in Chapter 13.

**Table 57.1** *Comparison of Transperitoneal and Retroperitoneal Laparoscopic Pyeloplasty*

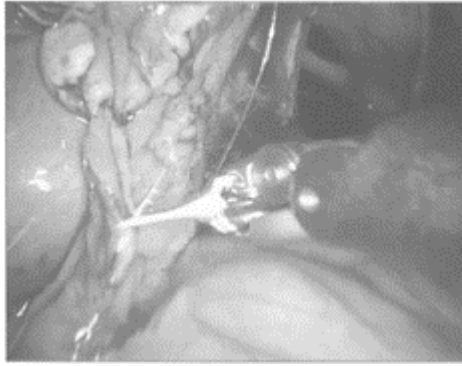
| Transperitoneal                                  | Retroperitoneal                                    |
|--|--|
| Greater working area                             | Direct access to UPJ                               |
| Transmesenteric direct access to UPJ possible    | Avoid direct contact with intraperitoneal contents |
| Port placement and access more rapid             | More readily drained post-op                       |
| Direct visualization of intraperitoneal contents | Any urine leak contained                           |
| Best approach for initial learning               |  |

Retroperitoneal pyeloplasty is usually performed in the lateral position; however it can be performed in the prone position, providing direct access to the renal pelvis, but offering a more limited working space. The procedure is otherwise identical to transperitoneal repair.

With the emergence of clinically useful robotic devices to assist in laparoscopic surgery, laparoscopic pyeloplasty in children can become more widely performed. By providing enhanced vision, including magnified three-dimensional images, full range of motion manipulating devices at the ends of laparoscopic instrument arms and a very natural feel for the operator, pyeloplasty even in the small child can be readily accomplished. This has largely been performed transperitoneally due to the larger size of the instruments, but as these are being scaled down, retroperitoneal access in small children will be feasible. The exposure and operative steps are essentially identical to conventional laparoscopic pyeloplasty (Figures 57.2 and 57.3) Early experience has shown excellent results with improving efficiency.<sup>62</sup>

**Fenger-plasty**

An alternative, nondismembered, method of correcting UPJ obstruction has been described based upon the Heineke-Mikulicz principle,<sup>63</sup> which involves a longitudinal incision through the stenotic segment of the ureter that is closed simply in a transverse direction. This is obviously well suited to laparoscopic methods as it has a limited amount of suturing. The clinical data on its efficacy are limited, however. A few reports of its use in laparoscopic applications have been presented.<sup>56,64,65</sup> To date, the data are not very convincing that this is a broadly



**Figure 57.2**

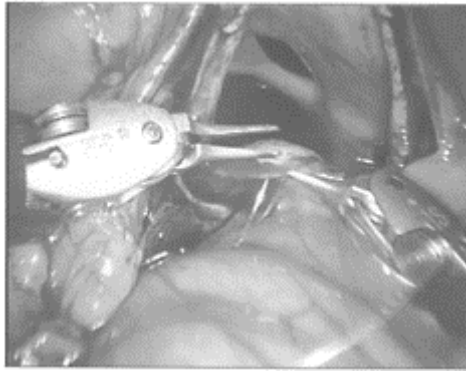
Robotic pyeloplasty using the daVinci surgical robot. The ureter has been spatulated and the vertex suture is being placed.

useful method of correcting pediatric UPJO. One concern is the means by which the complex anatomy often seen in children is handled. Many children, as noted above, have a tortuous UPJ that is not readily amenable to a simple longitudinal incision. If the operator is not comfortable with alternative means of pyeloplasty, how would such a case be handled intraoperatively as the anatomy is unknown until the UPJ is exposed? Similarly, with a crossing vessel that necessitates transposition of the ureter, this approach is of no value. Since the identification of a crossing vessel preoperatively is imperfect, the utility of this method is limited.

### Ureteral polyps

Endourologic management of ureteral polyps has been described in one child.<sup>38</sup> At the time of a laparoscopic pyeloplasty, the polyps could be readily removed and would not pose any problem with repair, just as with open pyeloplasty. In the less complex techniques, it would be important to recognize the possibility of polyps and be able to recognize them if present. In general, simple resection is adequate and no formal change in the reconstruction is needed. It would seem reasonable to proceed with a formal repair of the UPJ in any event, as there is some suggestion that the polyp is a secondary process to obstruction in a peristalsing lumen. Whether that is a universal observation is uncertain, but it would seem the safest approach to assume an obstruction complicated by polyp, and thereby to repair both, than assume the polyp as the only factor in the obstruction and risk the need for reoperation.





**Figure 57.3**

Robotic pyeloplasty using the daVinci surgical robot. A 5-0 absorbable suture is being passed through the posterior aspect of the renal pelvis for the beginning of the anastomosis. The exposure is transperitoneal.

### **Secondary ureteropelvic junction obstruction**

#### *Strategies*

While identification of the patient with a failed pyeloplasty may be very obvious, at times this may be as challenging as with the initial diagnosis in the asymptomatic patient. If pain, persistent leakage or marked increase in hydronephrosis occurs, some early intervention is needed. More often, there is very slow improvement in the degree of dilation, or lack of improvement in the washout parameters on diuretic renography. In the asymptomatic patient one must factor in the degree of initial dilation, the age of the patient, and the nature of the obstruction. The most rapid improvement in dilation is seen in the young patient with moderately severe dilation, especially associated with a crossing vessel, while the most delay is seen in the older child with massive dilation and an intrinsic narrowing. We usually perform a postoperative ultrasound at 1 month and, as long as the degree of dilation is no more than preoperative, that is considered a satisfactory result. If there is more dilation or symptoms develop, a functional study such as an IVP or diuretic renogram is performed to make sure there is not a high-grade obstruction.

In the setting of a symptomatic patient or in whom there is clearly severe ongoing obstruction; an early intervention as described below is performed. If the results are ambiguous, a further period of observation is appropriate, as it is well known from the days of routine nephrostomy use in pyeloplasty that delayed opening of the UPJ after

successful repair is frequent, and not of great risk. This might be a follow-up ultrasound or repeat functional study. Invasive evaluation such as retrograde pyelography or percutaneous antegrade studies are reserved for patients warranting intervention.

### *Therapeutic options and decision making*

If it is determined that the result of the pyeloplasty is inadequate, intervention is appropriate and can be either retrograde stenting or antegrade drainage and possible stenting. Very early stenting is difficult and risks disruption of a repair that is only transiently obstructed. Therefore, an antegrade approach is preferred, usually with a temporary nephrostomy for drainage. Passage of contrast by the repair is assessed after the period of drainage, as the repair may open spontaneously after taking the pressure off. If still closed, an antegrade stent may be placed for passive dilation.

For persistent UPJO more than 3 months post-operative, retrograde assessment, dilation, and stenting are reasonable options. There are no good data in children regarding optimal timing or duration of such stenting maneuvers. Dilation is best achieved using a small, 8 F, dilating balloon (Microvasive, Watertown, Massachusetts), followed by stenting with a 5–6 F double-J stent, or a nephroureteral stent if approached antegrade. The limitation of the double-J stenting approach is that access to the ureter is lost with testing patency, unless an antegrade nephrostomy is left in place. Parallel nephrostomy and ureteral stenting can be used, but this is cumbersome. A nephroureteral stent (e.g. Salle stent; Cook, Spencer, Indiana), replaced by a simple nephrostomy, may also be used. With this arrangement, the patency of the anastomosis may be tested and assured prior to removing a drainage tube. It is best to clamp the nephrostomy temporarily to ensure asymptomatic adequate drainage.

Endopyelotomy for persistent UPJO has been described and has its proponents. The usual approach is through retrograde incising balloon (Accusize, Applied Medical), although the large size (10 F deflated, 24 F inflated) of the instrument limits its utility to teens. Stenting for 2–4 weeks after is recommended. There are limited follow-up data and our institutional experience is less than enthusiastic. Open repair after endopyelotomy is often challenging, due to the inflammatory effects of the obligate extravasation induced.

Direct vision endopyelotomy is also an option from an antegrade approach, but again there are few data and limited experience. These approaches are generally worth an attempt after careful discussion with parents who are already frustrated. In many cases a more definitive approach of reoperative open or laparoscopic pyeloplasty is most advisable. The anticipated success rate is probably in the 85% range for open reoperative pyeloplasty, but there are very few reports, and none for pediatric redo laparoscopic pyeloplasty.

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## Anomalies of the lower ureter: minimally invasive treatment options

Lars Cisek

The ureter is the conduit for urine in its path to the bladder. Consequently, ureteral anomalies are poised to disrupt this transit and therefore compromise renal function. This chapter will focus on problems of the ureter itself leaving abnormalities of the proximal junction (UPJ) and distal anomalies such as reflux to other chapters of the book.

### Ureteral stricture, valves, and folds

This category represents a rare cause of functionally significant ureteral obstruction in children. Congenital ureteral strictures represent a fixed anatomic narrowing of the ureter;<sup>1,2</sup> this may occasionally present with multiple lesions in the same ureter. Further, dilation of the segment between narrowed regions may occur. Ureteral valves represent a transverse fold of mucosa containing muscle,<sup>3,4</sup> and are obstructive entities. More common are mucosal folds, although these are seldom the source of true obstruction.<sup>4,5</sup> These lesions represent redundancy of the mucosa, which most often resolves spontaneously over time. This later lesion can be seen in IVPs distorting the ureteral contrast column; the critical feature is the absence of obstruction. It is important to note that folds and valves may be the result of tortuosity of the ureter proximal to an obstruction, and may themselves not be obstructive.<sup>6</sup>

In cases with functionally significant obstructions, presentation may be through incidental finding, infection, flank pain, hypertension, or the finding of (prenatal) hydronephrosis and associated proximal ureterectasis. Ultrasonography will demonstrate proximal dilation (of both the ureter and kidney) without distal ureteral dilation. Evaluation of the function of the affected renal unit may show reduced functional contribution. In flow-dependent nuclear imaging, the dilated proximal ureter may be seen, and the clearance ( $T_{1/2}$ ) will be prolonged. Similarly, an anatomic study such as an IVP will demonstrate proximal dilation, define the location of the narrowing, and facilitate operative planning. The need for intervention is based on findings of obstruction coupled with symptoms—e.g. urinary tract infection (UTI), pain—or evidence of functional impairment of the kidney in obstructed but otherwise asymptomatic cases.

Therapeutic options are analogous to the treatment of acquired strictures. Options include balloon dilation, ‘endopyelotomy’ methods, laparoscopic or open uretero-ureterostomy, transuretero-ureterostomy, psoas hitch with reimplant, or nephrectomy. Nephrectomy is appropriate in cases of minimal renal function in the affected side. In patients with short lesions (<2 cm) or greater than 25% renal function, endoscopic means

may be considered<sup>7</sup> if appropriately sized instruments are available. One caution in considering these techniques in children is that the often generous 'cushion' of retroperitoneal fat that isolates the ureter from adjacent structures (bowel, vessels) in adults provides a far smaller margin of safety for most children. The size of instrumentation is the other significant limiting factor; at present, common commercial ureteroscopes are in the 7 F range and the smallest currently available cutting balloon is 10 F (Applied Medical—Acusize). Biliary sphincterotomes without balloons could be considered and are available to 3.5 F. Of note, a ureteral valve is a pathology conceptually best addressed by incision. In this entity, the mucosal flap/fold is the issue and intraureteric mucosal and muscle incision alone should repair this. At present, there are essentially no available data in children to guide the urologist in the success rate for minimally invasive approaches for these problems. All recommendations are derived by analogy from adults.

'Endopyelotomy' methods demonstrate success rates in the 55–85% range for strictures shorter than 2 cm in adults.<sup>8–10</sup> Laparoscopic series are rare in the literature, although Nezhat et al<sup>11</sup> reported a 77% success rate with ureteroureterostomy in a group of 9 patients with iatrogenic injuries.

#### *Acusize or balloon dilation ureteral stricture or valve method*

- Equipment: fluoroscopy, cystoscope, acusize balloon, guide wires, contrast media, appropriate length double J stent.
- Preoperative: urine culture and treatment of any current UTI. Magnesium citrate or bisacodyl bowel preparation 1 day preoperatively for improved radiologic visualization. Antibiotic prophylaxis.
- Position for fluoroscopy.
- Cystoscopy with retrograde pyelogram, define site(s) of obstruction.
- Place wire past obstruction.
- Place balloon/acusize catheter over the working wire.
- Advance to the position of the ureteral narrowing, following the bracketing markers on the balloon to center on the site of the obstruction.
- Inflate, cutting current with orientation based on location (proximal to iliac vessels—posteriolateral; vessel—anterior; distal to iliac vessels—posterior).
- Contrast injection looking for extravasation if cutting for stricture. Note: for a ureteral valve, full-thickness incision is not required.
- Place stent for 4 weeks. (If valve may stent for 1 week only.)
- Remove stent and confirm patency with retrograde pyelogram/balloon calibration.
- Follow up with renal ultrasonography (RUS) at 1 month if clinically well. Failure of hydronephrosis to improve should prompt reinvestigation.

#### *Endoscopic incision method*

- Equipment: Fluoroscopy, cystoscope, guide wires, ureteroscope, holmium laser source and fiber, contrast media, double J stent.

- Preoperative: urine culture and treatment of any current UTI. Magnesium citrate or bisacodyl bowel preparation 1 day preoperatively for improved radiologic visualization. Antibiotic prophylaxis.
- Position for fluoroscopy.
- Cystoscopy with retrograde pyelogram to define anatomy.
- Place wire/safety wire.
- Dilate ureteral orifice if needed. Note it may be necessary to 'pre-stent' smaller patients to gain access to the ureter without unnecessary trauma. This should be short duration only to preserve proximal dilation so as to be able to clearly identify the location of narrowing.
- Advance ureterscope to region of narrowing.
- Visualize obstructing region.
- Incise with holmium laser to visualize fat in the retroperitoneum. Note: for a ureteral valve, full-thickness incision is not required (proximal to iliac vessels—posteriolateral; vessel—anterior; distal to iliac vessels—posterior).
- Place stent for 4 weeks. (If valve may stent for 1 week only.)
- Remove with retrograde pyelogram/balloon calibration.
- Follow up with RUS at 1 month if clinically well. Failure of hydronephrosis to improve should prompt reinvestigation.

#### *Laparoscopic ureteroureterotomy method*

- Equipment: fluoroscopy, cystoscope, guide wire, contrast media, ureteral occlusion balloon catheter, double J stent, 3 laparoscopy ports (3–5 mm format; typically, short length preferred), 5 mm Babcock, 3 mm needle driver, 3 mm scissor, 3 mm grasper, scissor, and dissector, 6–0 absorbable suture on BV-1 or TF needle, a bipolar cautery or harmonic scalpel will be useful. We prefer the use of Koh (Storz) instruments for fine suturing tasks as these instruments will handle 6–0 and 7–0 suture and fine needles well.
- Preoperative: magnesium citrate or bisacodyl bowel preparation 1 day preoperatively.
- Position for fluoroscopy.
- Cystoscopy with retrograde pyelogram to define anatomy.
- Place occlusion balloon above stricture and inflate. With balloon inflated, confirm a 'snag' at the region of identified stricture. Fix position thoroughly by securing to Foley catheter at bladder neck.
- Position patient with a 30° roll, contralateral side down. Secure to table to allow full range of motion. Maintain capacity for fluoroscopy and dye injection to confirm location of pathology, if needed. Catheter should be accessible from field to manipulate.
- Access abdomen.
- Port placement based on site of stricture. Port sites can be either 3–3 mm, mixed size 3 mm and 5, or 3–5 mm. We prefer one 5 mm (which allows the use of a 5 mm Babcock to handle the ureter) and two 3 mm ports.
- The ureter can usually be easily observed in children directly through the retroperitoneum and mesentery and the site of the balloon localized visually. Expose the ureter, limiting the mobilization of the ureter to preserve blood supply. Confirm



site of stricture via a balloon tug. Repeat retrograde pyelogram via wire port if needed. In some cases it may be necessary to reflect the colon.

- Place marking suture(s) to define position and manipulate the ureter; avoid the balloon.
- Ureterotomy at the site of narrowing. Identify the valve or stricture. If a true stricture, remove involved segment. If a valve is present, opening the ureter through the region of the valve is the critical feature, with incision, although the valve with Heineke-Mikulicz closure is sufficient.
- Reattach or close the ureter using intracorporeal 6–0 Monocryl or PDS (on BV-1 needles) interrupted sutures. Rotation of the ureter by 120° or less is of no apparent consequence.
- A stent is typically used. Place wire from below, following back wall closure. The wire may be introduced via an occlusion balloon wire port.
- A drain may also be placed. At minimum, either a drain or a stent is required. If a drain is chosen, a 3 mm port can be placed posteriorly and advanced to the peritoneum. Once the peritoneum tents, the trocar is removed and the port advanced through the retroperitoneum to the region of the anastomosis. A 7 F round JP drain can be introduced via one of the other port sites, grasped and delivered through skin using this port site.
- Close the retroperitoneum if windowed or reattach colon if reflected.
- Remove ports under direct vision. In children, it is our practice to close all ports where the fascia can be seen regardless of size. We close the fascia of all port sites 5 mm or greater.
- Follow up with RUS at 1 month if clinically well. Failure of hydronephrosis to improve should prompt reinvestigation.

### Ureterocele

A ureterocele is a submucosal cystic dilation of the terminal segment of the ureter. There are several classifications for ureteroceles:<sup>12,13</sup>

- Intravesical or extravesical—located within or distal to the bladder, respectively.
- Solitary system or duplex—associated with a single renal collecting system or the upper pole of a duplex system, respectively.
- Orthotopic or ectopic—insertion of the ureter into the bladder in the normal or distal (i.e. medial and inferior) position. The orthotopic ureterocele is usually found associated with a single renal unit with one collecting system and is more common in adults.
- Cecoureteroceles are elongated beyond the ureterocele orifice by tunneling under the trigone and the urethra.<sup>13</sup> These may commonly be obstructive at the bladder neck.

With the increasing use of prenatal ultrasound, many ureteroceles are now detected as prenatal hydronephrosis.<sup>14</sup> The findings include hydronephrosis and a fluid-filled structure within the bladder. The most common clinical presentation of a ureterocele postnatally is a UTI with sepsis in the first few months of life.<sup>15,16</sup> Patients may also present with hematuria, purulent urine, pyelonephritis, or abdominal pain.<sup>17</sup> Urinary

incontinence or retention may also be seen if the ureterocele causes an obstruction at the level of the bladder.

### *Evaluation*

Ultrasonography noninvasively depicts anatomic changes in the kidney and bladder. Imaging should be performed with the bladder empty and filled to eliminate nonvisualization of ureteroceles due to either compression of the bladder or the ureterocele. Sonography is the most sensitive test and often the only radiologic evaluation required for the diagnosis of ureteroceles. A ureterocele is seen as a fluid-filled cystic intravesical mass. It is also known as a 'cyst within a cyst.' Ureteroceles may be missed if the patient's bladder is empty or fully distended, if the ureteroceles are small, or if the patient's body habitus precludes proper examination. Ultrasonography also defines the degree of hydronephrosis, and it possibly depicts renal dysplasia or cortical thinning. With their distinct split renal pelvises, duplex renal systems may also be identified on the initial ultrasonographic examination.<sup>18</sup> The finding of upper pole hydronephrosis and a dilated ureter should prompt careful inspection of the bladder for a ureterocele.<sup>19</sup>

Because of the association with reflux (vesicoureteral reflux is present in about 50% of ipsilateral lower pole moieties in duplex systems and 10–25% of contralateral moieties in single and duplex systems,<sup>14,20</sup> a voiding cystourethrogram (VCUG) is necessary. The presence of reflux will favor bladder level management of the ureterocele. Early imaging prior to complete opacification of the bladder with contrast material may show the ureterocele as a filling defect. VCUG defines the degree of vesicoureteral reflux in both ipsilateral and contralateral systems and also possible inferior displacement of the lower pole to a large obstructed upper pole. The drooping lily sign is a classic description of moderate-to-high-grade reflux into a displaced lower pole.

In addition, VCUG may be performed to evaluate the size, position, tension, degree of detrusor backing, and compressibility of ureteroceles. Eversion of ureteroceles on VCUGs may be seen as protrusions outside the urethral or vesical wall.<sup>21</sup>

A functional study (DMSA or MAG3) is indicated in those cases with significant obstructive components in the upper pole moiety associated with the ureterocele, as minimal function favors excision of the affected kidney and ureter.<sup>22</sup>

Treatment options must be individualized, based on the unique anatomy, pathophysiology, and renal function found in the patient with a ureterocele. Treatment often involves surgical intervention. The anatomy of the urinary tract must be delineated as clearly as possible prior to surgical intervention. Ipsilateral and contralateral renal function must be assessed. The four goals of intervention are:

1. control and elimination of infection
2. minimization of vesicoureteral reflux and bladder outlet obstruction
3. maintenance of urinary continence mechanisms
4. preservation of renal function.

### *Medical therapy*

Mere observation is rarely a good option in symptomatic ureteroceles. Antibiotics should be instituted during the initial diagnostic evaluation and during surgical intervention for

both pediatric and adult ureteroceles. In infants with symptomatic ureteroceles, antibiotics should be used to treat UTIs. Following therapy, antibiotic prophylaxis is instituted, and may be used to delay surgical intervention until the bladder matures. Small asymptomatic ureteroceles may be observed with careful serial physical and ultrasonographic examinations.

### *Surgical therapy*

Surgical options include endoscopic ureterocele incision, and, depending on renal function, percutaneous diversion, ureteropyelostomy, partial or total nephroureterectomy, or complete reconstruction. At present, minimally invasive approaches that aim to address the problem at the 'lower tract' level are limited. In complete reconstruction, the approach is often a combined approach with minimally invasive upper tract surgery coupled with open bladder level reconstruction.

Indications for surgical treatment for both pediatric and adult ureteroceles depend on the site of the ureterocele, the clinical situation, associated renal anomalies, and the size of the ureterocele. Common indications are reflux, infection, obstruction (both of the associated renal moiety and potentially bladder outlet), and impairment of continence. The surgical approach is individualized, and is based upon the following: age of the patient, size and location of the ureterocele, renal function, presence and degree of vesicoureteral reflux, and comorbid conditions (risk of anesthesia).<sup>23</sup>

Surgical therapy for both pediatric and adult ureteroceles may include endoscopic incision or transurethral unroofing of the ureterocele in the adult patient, upper pole heminephrectomy and partial ureterectomy with ureterocele decompression, ureteropyelostomy, excision of ureterocele and ureteral reimplantation, and nephroureterectomy. There is a significant debate as to whether management should be 'lower tract' or 'upper tract' based. In general, the moiety associated with the ureterocele is not a significant contributor to renal function, and the approach should eliminate problems with obstruction while correcting any concurrent issues (reflux).

A useful guide to therapy proposed by Churchill et al<sup>24</sup> can be used to guide therapeutic considerations in children:

#### *1. Upper pole nonfunction*

- One renal unit in jeopardy—only the upper pole drained by the ureterocele is affected (other renal units normal, may have grade I-II vesicoureteral reflux): perform upper pole heminephrectomy.
- Entire ipsilateral renal unit or all renal units in jeopardy—ipsilateral and/or contralateral renal units affected by hydronephrosis or high-grade vesicoureteral reflux: perform upper pole nephroureterectomy, ureterocele excision with ureteral reimplantation.

#### *2. Indeterminate function*

- Perform endoscopic incision and reassessment of function.

#### *3. Upper pole function present*

- One renal unit in jeopardy: perform ureteropyelostomy and ureterocele drainage.

- Entire ipsilateral renal unit or all renal units in jeopardy: perform ureteropyelostomy, ureterocele excision, and ureteral reimplantation.

*Note:* the endoscopic incision is also considered first in infants who are medically unstable because of sepsis or coexistent medical conditions.

### **Endoscopic incision**

Endoscopic incision is the least invasive method for decompressing the ureterocele. It is an ideal method for dealing with a neonate with ureterocele-induced obstructive uropathy and sepsis. Other indications are a single-system intravesical ureterocele with obstruction or a duplex-system ureterocele with indeterminate function of the affected renal moiety. In the endoscopic approach, a small endoscopic incision is made inferiorly and medially on the anterior wall of the ureterocele above its base at the bladder neck.<sup>25–27</sup> This minimally invasive method is associated with low morbidity rates and represents an effective method of decompression in infants. The incision is designed to effect drainage without loss of a ‘flap valve’ function and resultant creation of reflux. The endoscopic approach is highly successful for small, single-system intravesical ureteroceles.<sup>27</sup> With this procedure, the reported incidence of iatrogenic reflux and incontinence (<10%) is low, and secondary procedures are often not needed (10–15%).<sup>25,26</sup> The endoscopic approach represents a good first-line method for the acute management of symptomatic ureteroceles. In particular, as regards an infected renal unit, it serves as the method of first choice to relieve the obstruction.

In addition to its therapeutic value, this technique may be employed when the contribution of the associated renal moiety to overall renal function is uncertain. Improvement in renal function after an incision indicates that reconstruction is favorable, if necessary, and poor function indicates that excision of the upper pole moiety is preferable. This procedure allows palliative decompression in children at high risk (secondary to concurrent medical illness), so that definitive reconstruction can be delayed until an adequate healing period has occurred. This decompression may allow the ureter to reduce in size, facilitating reconstruction. This approach is seldom definitive in those patients with reflux, who will likely require lower tract reconstruction.<sup>28</sup>

### **Transurethral unroofing**

Transurethral unroofing of a ureterocele reliably achieves decompression and allows effective treatment of infection in symptomatic ureteroceles, but invariably results in reflux into the affected moiety. The potential for vesicoureteral reflux limits the use of endoscopic unroofing in children to infection control.

### **Upper pole heminephrectomy and ureterectomy**

Upper pole heminephrectomy and partial ureterectomy with ureterocele decompression involves removal of the upper pole of the kidney, as well as the affected proximal ureter to a position as distal as is reasonable. The remaining distal ureterocele is not excised but rather is decompressed. This is approached as definitive treatment in patients with an obstructed ectopic ureterocele and a dysplastic upper pole, but without associated

vesicoureteral reflux. If reflux is present preoperatively, the distal ureter should be ligated rather than allowing it to remain decompressed. Nephroureterectomy is performed in patients with single-system ureterocele and a nonfunctioning kidney.

This operation has been noted to cause spontaneous resolution of ipsilateral vesicoureteral reflux and contralateral reflux and/or obstruction. Upper pole heminephrectomy and partial ureterectomy with ureterocele decompression has been reported to cause spontaneous resolution of grade I and II vesicoureteral reflux in 60% of cases, while higher grades of reflux necessitated bladder reconstruction in 96% of cases. While upper pole heminephrectomy provides effective decompression, the likelihood of subsequent bladder surgery may be significant, especially if reflux is already present.<sup>29–33</sup>

Factors that may predict the likelihood of future surgical intervention include high-grade reflux (grades III, IV, V) and poor detrusor backing behind the remaining ureterocele.<sup>32,33</sup> Therefore, upper pole heminephrectomy is an excellent first-line procedure for the child with a ureterocele that affects only the ipsilateral upper pole. It is a good choice in the child with a ureterocele with only ipsilateral renal involvement (which may include upper pole obstruction and lower pole reflux, for example). In any case, the patient and family should be counseled about the potential need for further surgical procedures.

This upper tract approach is ideally suited to a laparoscopic approach, as access to the kidney and ease of defining the associated vascular anatomy is excellent. It also allows access to the entire upper pole ureter, facilitating removal.<sup>34–37</sup>

### **Ureteropyelostomy**

Ureteropyelostomy joins the upper pole ureter to the lower pole renal pelvis. This is preferred if the affected renal unit demonstrates significant function and no reflux or obstruction is present. Alternatively, a high ureteroureterostomy will achieve similar ends. This bypasses the obstructing distal problem, and is an option if upper pole function is significant. This upper tract solution can also be effected efficiently through a laparoscopic approach, although no reports of ureteropyelostomy or ureteroureterostomy have yet been made for this indication.

### **Excision of the ureterocele and ureteral reimplantation**

Excision and ureteral reimplantation is the primary procedure of choice if the patient has significant vesicoureteral reflux in the lower pole moiety and a well-functioning upper pole moiety and/or significant contralateral vesicoureteral reflux. Both ipsilateral ureters may be reimplanted within a common sheath or via uretero-ureterostomy. Note the common sheath reimplantation has a distinct disadvantage of reimplanting a very dilated distal upper pole ureter into the small bladder. The decision whether to taper the ureters must be made on an individual basis. This operation is commonly delayed until the child is older (approximately 2 years old); however, the operation should be performed before the child is toilet trained, since it has a significant potential to be disruptive to or alter urinary continence.

In the pediatric population, the excision and reimplantation procedure is commonly employed as a secondary procedure (after previous heminephrectomy or endoscopic

incision of a ureterocele) because of UTI, voiding disturbance, persistent vesicoureteral reflux, or obstruction. Significant vesicoureteral reflux on initial VCUG usually indicates that lower tract reconstruction will be necessary. Of note, if this procedure is selected as the first-line treatment in the appropriate patient, the rate of secondary surgery is low.

A lower tract reconstruction approach has not yet been reported using laparoscopic techniques.

### Total reconstruction

The traditional method of correcting an ectopic ureterocele in a duplex system has been to perform a total reconstruction. This involved surgery at both the bladder and renal level. The bladder surgery required excision of a ureterocele, reconstruction of the detrusor, and reimplantation of the ipsilateral ureter. This was followed by a flank incision and upper pole heminephrectomy.<sup>38</sup> Since most ureteroceles typically present in young children (often <1 year old), total reconstruction is technically challenging, and complications were common. This lends itself well to a combined approach where the upper tract surgery is done laparoscopically and the ureter and upper pole moiety are placed in the pelvis for removal through a conventional Pfannenstiel incision used to effect the lower tract reconstruction.

**Preoperative details.** The goals of the preoperative evaluation of the ureterocele are as follows:

- detailed delineation of upper and lower urinary tract anatomy
- estimation of differential function of all renal moieties
- determination of the presence of obstruction (anatomic or functional) or vesicoureteral reflux.

### Endoscopic incision of the ureterocele

This is the least invasive technique. The patient is placed in the lithotomy position. Cystoscopy is performed, and any issues related to the location of the ureteral orifice or anatomy can be resolved concurrently. Incision of the ureterocele is performed via the pediatric resectoscope or a cystoscope using a small Bugbee electrode (3 F) and a cutting current. Create a small puncture at the lowest point (most distal edge) just above the base of the ureterocele. The endpoint of the incision is observation of a clear jet of urine from the ureterocele or ability to visualize the urothelium on the inside of the ureterocele. A retrograde can be performed if any question remains.

Note the ability to visualize the ureterocele is dependent on the degree of bladder filling as the ureterocele will efface as the bladder fills. The procedure is best done at minimum bladder filling to allow visualization of the bladder and ureterocele.

**Postoperative details.** A dose of intravenous antibiotics is given perioperatively unless concurrent infection is present, in which case ongoing therapy is employed. Prophylaxis is used following discharge until reflux status is confirmed.

**Follow-up care.** Follow-up care consists of serial monitoring of renal function, periodic evaluation of voiding symptoms and bladder function, and interval radiologic studies to assess renal growth, hydroureteronephrosis, and vesicoureteral reflux. A typical schedule in the absence of infection or other problems is an ultrasound at 2–4 weeks and VCUG

and ultrasound at 3–6 months postoperatively. If reflux is absent, prophylaxis can be discontinued.

### **Laparoscopic nephroureterectomy**

This procedure is employed for a single-system ureterocele associated with nonfunction of the renal unit.

**Equipment.** Laparoscopic ‘cart’, Visiport (USSC, Norway, Connecticut), harmonic scalpel, 5 mm clip applier, 10 mm entrapment sac (often not required), grasper, dissector, scissors.

**Operative steps.** For prone retroperitoneoscopic nephrectomy:

1. Patient positioned prone and secured, with support at iliac crests and axilla.
2. Confirm lack of pressure or limitation of forward fall of abdomen.
3. Visiport access, costovertebral angle inferior to 12th rib and lateral to sacrospinalis.
4. Gentle pressure on Visiport to keep against sacrospinalis, orientation of blade in sagittal plane.
5. No muscles traversed, incise fascia of erector muscle, sacrospinalis medial, open fat lateral.
6. Come to lumbodorsal fascia, incise, quadratus lumborum in front of lens, drift Visiport laterally slightly, incise.
7. Once retroperitoneal fat seen, orient scope towards psoas, pointing to pelvis, initial dissection of space.
8. If balloon desired, place and inflate (5 min for minor vessel tamponade).
9. Fully free space with 10 mm lens, identify peritoneum and psoas.
10. Increase pressure to 15 mmHg.
11. Place two 5 mm working ports, incise skin 3–7 mm stab wound: one 1–2 cm above iliac lateral to sacrospinalis; one 1–2 cm above iliac at posterior axillary line, avoid transgressing the peritoneum which has been actively reflected as far anteriorly as possible.
12. Suture secure all ports.
13. Reduce pressure to working level.
14. Grasper/dissector and scissors to working ports.
15. Dissection anterior to (‘below’) 10 mm port lower pole of the kidney located here.
16. Dissect lower pole free, move superiorly to free posterior aspect of kidney.
17. Find ureter by dissection medially from the lower pole.
18. Follow ureter superiorly to hilum.
19. Additional dissection of kidney will tend to allow kidney to fall laterally.
20. Free hilum, identify artery and vein, dissect artery free.
21. Suction aspirate to keep field highly visible.
22. Clip renal artery, proximal and distal.
23. Observe kidney to loss of perfusion, identify additional arteries as needed.
24. Divide arteries which have been clipped.
25. Dissect renal veins, apply clips, proximal and distal.
26. Divide veins.
27. Mobilize, free kidney from attachments anteriorly, maintain caution for missed or upper pole vessels.

28. Once fully mobile, dissect ureter distally as far as possible (to level of vas in males, to bladder in females), once secure end length, may divide proximally prior to continued distal dissection/ligation.
29. Divide ureter, electrocautery for nonrefluxing, EndoLoop for refluxing units.
30. Irrigate field.
31. Reduce pressure, confirm hemostasis.
32. Switch to 312–13 mm lens.
33. Return to normal working pressure.
34. Specimen extraction, via 10 mm port site: direct for small specimen, small extension of incision or entrapment sac for larger specimen.
35. Remove kidney.
36. Reduce pressure to reconfirm hemostasis.
37. Insufflate.
38. Remove ports.
39. Remove two 5 mm ports, direct vision closure of 10 mm port.
40. Suture incisions and close with benzoin and Steri-Strip.

**Postoperative details.** Only single-dose perioperative intravenous antibiotics are used unless a concurrent infection is suspected, in which case a longer course is used.

**Follow-up care.** In the absence of contralateral reflux/anomaly, follow-up is restricted to the immediate postoperative period. Late complications are unusual, and the procedure is typically definitive.

### **Upper pole heminephrectomy, partial ureterectomy with ureterocele decompression**

Partial nephrectomy to remove a dysfunctional upper pole segment is similar to that noted above, and consists of identification of the upper and lower pole vessels and ureter. Once the structures are sorted to upper or lower pole, division of the vessels to the dysfunctional segment, and division of the renal cortex along the line of demarcation identified following ligation of the associated vessels is performed.

The procedure follows the same approach as nephrectomy, except that identification of upper and lower segments and their vascular supply is critical. A harmonic scalpel is an excellent device to divide the parenchyma while avoiding hemorrhage. Typically, if the upper pole vasculature is divided prior to incising the renal parenchyma, no significant bleeding is encountered.

In mobilizing the ureter, care must be taken to avoid stripping the blood supply to the lower pole ureter. Dissection should take place directly on the surface of the upper pole ureter. Injury to the upper pole ureter is inconsequential. The ureter is mobilized distally as far as possible, then divided, as noted for nephrectomy. This can usually be done at a position at the level of the trigone. If difficulty separating the ureters due to an adherent common sheath or common wall is encountered, it is best to terminate distal dissection and divide the ureter.

**Postoperative details.** Intravenous antibiotics are continued until the patient is discharged from the hospital. Prophylaxis is used following discharge until reflux status is confirmed. Urethral catheters are removed when urine is clear. It is not uncommon for a fever to be present postoperatively and speculation as to the possibility of a portion of



devitalized upper pole tissue as the genesis of the trouble can be entertained. If the fever is high grade or protracted, evaluation with computed tomography (CT) or ultrasound is indicated.

**Follow-up care.** Follow-up care consists of serial monitoring of renal function, periodic evaluation of voiding symptoms and bladder function, and interval radiologic studies to assess renal growth, hydroureteronephrosis, and vesicoureteral reflux. A typical schedule in the absence of infection or other problems is an ultrasound at 1 month and VCUG and ultrasound at 3–6 months postoperatively. If reflux is absent, prophylaxis can be discontinued. Issues under evaluation are resolution or development of ipsilateral reflux and evidence of unimpaired drainage from the lower pole system.

### Ureteropyelostomy

In this procedure we anastomose the upper pole ureter to the lower pole renal pelvis in a fashion analogous to a pyeloplasty. This is typically approached in transperitoneal fashion to afford a larger working environment for intracorporeal suturing. A stent is typically placed, and this can be placed cystoscopically at the start of the procedure or percutaneously after the pelvis is opened. This procedure at present is currently best restricted to children >15 kg because of working space limitations in smaller children.

**Operative steps.** For laparoscopic ureteropyelotomy:

1. Patient positioned supine and secured, 30° wedge under ipsilateral side or full flank position.
2. Roll table 30° away from surgeon to ‘flatten’ patient.
3. Obtain access to peritoneal cavity.
4. Increase pressure to 15–20 mmHg.
5. Transilluminate abdominal wall for vessels.
6. Place working ports, incise skin 7 mm incisions, ipsilateral mid-upper abdomen at the paramedian position, ipsilateral mid-lower abdomen lateral to the rectus.
7. Suture secure all ports.
8. Reduce pressure to working levels.
9. Roll table 30° towards surgeon.
10. Grasper/dissector and scissors to working ports.
11. Divide ipsilateral line of Toldt, reflect colon medially. A mesenteric window may be used if the region of the UPJ can be visualized.
12. Expose kidney, freeing medially at the lower pole to begin exposure of hilum.
13. Attention towards lower pole to identify ureters, dissect ureters free. Follow this superiorly to the lower pole renal pelvis.
14. May place two 5 mm additional working ports: anterior to mid axillary line for additional working points.
15. Anterior-lateral traction on ureter to better expose hilum.
16. Free hilum, to expose the lower pole pelvis and UPJ.
17. Suction aspirate to keep field highly visible.
18. Place a hitch stitch in the pelvis to lift and secure the pelvis towards the midpoint of the lower two ports. These ports are the working ports for suturing.
19. Open the renal pelvis above the UPJ.
20. Incise and divide the upper pole ureter at a position lined up with the pelvic incision.

21. Spatulate the upper pole ureter over a matching length to the pelvis incision.
22. A single suture is placed in the crotch of the ureter spatulation to the dependent portion of the pelvis and tied. The suture is left with a tag to identify this position.
23. The back wall is sutured with a running stitch, and tied at the superior apex.
24. A ureteral stent is introduced if it was not previously placed by use of a 2 mm trocar placed at the subcostal margin in the midclavicular line. The stent is advanced down the trocar directly into the ureter.
25. The upper loop of the stent is placed in the renal pelvis of the upper pole moiety.
26. The front wall of the new UPJ is closed with a running suture.
27. Reduce pressure to confirm hemostasis.
28. Return to working pressure.
29. A drain may be placed if desired.
30. Reduce pressure, reconfirm hemostasis.
31. Insufflate.
32. Secure fascia as appropriate: 10 mm sites in adults are best closed using direct vision closure, 5 mm ports do not require closure. In children, 5 mm ports should be closed.
33. Remove ports.
34. Suture incisions and close with benzoin and Steri-Strip.

**Postoperative details.** Intravenous antibiotics are continued until the patient is discharged from the hospital. Prophylaxis is used following discharge until reflux status is confirmed. Urethral catheters are removed when urine is clear. If an internal stent has been placed, it is removed 3–6 weeks after surgery. A postoperative ultrasound is obtained 1 month following the removal of the stent.

**Follow-up care.** Follow-up care consists of serial monitoring of renal function, periodic evaluation of voiding symptoms and bladder function, and interval radiologic studies to assess renal growth, hydroureteronephrosis, and vesicoureteral reflux. A typical schedule in the absence of infection or other problems is an ultrasound at 1 month and VCUG and ultrasound at 3–6 months postoperatively. If reflux is absent, prophylaxis can be discontinued.

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## Renal dysplasia and cystic disease

Alaa El-Ghoneimi

Renal dysplasia is a common kidney disorder. It is frequently associated with congenital obstructive uropathy that leads to renal failure in children.<sup>1</sup>

Despite the frequent occurrence of renal dysplasia in association with obstructive uropathy, its pathogenesis remains unknown. Abnormal metanephric differentiation in cases of renal dysplasia results in abnormal renal organization and poor development of renal elements. This abnormal differentiation may be secondary to a disturbance in the inductive interaction between the ureteric bud and the metanephric mesenchyma. It has also been suggested that renal dysplasia is not an end-stage phenomenon, but rather involves the abnormal expression of genes normally found in the cascade of renal differentiation, leading to malformed kidney. Various growth and transcription factors, including human growth factor, platelet-derived growth factor, fibroblast growth factor, keratinocyte growth factor, transforming growth factor, glial cell line-derived neurotrophic factor and their receptors are dysregulated in renal dysplasia.<sup>2-4</sup> This dysregulation may provide a continuous signal for proliferation, which may explain persistent dysplastic tubules in the postnatal period.<sup>3</sup>

Renal dysplasia is a histologic term defining a malformed part or the whole kidney and the presence of primitive ducts lined with undifferentiated columnar epithelium and surrounded by undifferentiated fibro-muscular collar with sometimes a metaplastic element such as cartilage.

Classically, kidney malformations including dysplasia are classified based on histology. Recent advances in molecular biology and genetics have led Woolf and Winyard to suggest a more straightforward classification to describe kidney malformations. The abnormalities can be divided into groups based on the underlying cell biology, such as aberrant early development or defects in terminal maturation.<sup>5,6</sup> The aberrant early development group includes dysplastic kidneys, whether large multicystic dysplastic kidneys (MCDKs) or small organs with a combination of hypoplasia/dysplasia and some obstructed kidneys.

Defects in terminal maturation are observed in polycystic kidney disease (PKD). Initial nephron and collecting duct malformation is unremarkable in these kidneys, but there is later cystic dilation of these structures, causing secondary loss of adjacent normal structures. The commonest types are the autosomal dominant and autosomal recessive PKD. Cyst decortication is sometimes indicated in adults and the laparoscopic techniques has been thoroughly described in cases of complicated cysts of PKD.<sup>7,8</sup> This category of renal diseases is usually not associated with obstructive uropathy and is mainly managed

by nephrologists for the development of renal failure and hypertension; their description is beyond the field of this chapter.

Dysplastic kidneys can be any size, ranging between massive kidneys with multiple large cysts up to 9 cm, which are commonly termed MCDKs, to normal or small kidneys, with or without cysts. Dysplasia can be unilateral, bilateral, or segmental, affecting only part of the kidney. Unilateral incidence is 1 in 3000–5000 births, compared to 1 in 10,000 for bilateral dysplasia.<sup>5,9</sup> MCDK can be familial, but is most commonly a sporadic anomaly. The mode of familial transmission can be an autosomal dominant inheritance with variable expressivity and reduced penetrance. Belk et al<sup>9</sup> did not find any significant renal anomalies in any of the 94 first-degree relatives of the MCDK index cases; therefore, formal screening of relatives is not recommended.

### Diagnosis

Commonly, dysplasia is applied to the bright echogenic appearance secondary to the lack of normal renal parenchyma and structurally abnormal kidney. Meanwhile, this ultrasonographic appearance is not pathognomonic to histologically defined dysplasia.<sup>10</sup> The current classic presentation of MCDK is the prenatal sonographic diagnosis. The typical sonographic appearance is a multiloculated abdominal mass consisting of multiple thin-walled cysts, which do not appear to connect (Figure 59.1). To be differentiated from hydronephrosis, no renal pelvis or parenchyma can be demonstrated in MCDK. Other sonographic patterns are circumferential cysts in kidneys of more normal size, particularly in bilateral cases associated with lower urinary tract obstruction. The amniotic fluid volume is usually normal in unilateral cases in contrast with bilateral cases, where oligo- or anhydramnios is the most common associated findings.<sup>11</sup> Small hypo/dysplastic kidneys are difficult to detect prenatally and in unilateral cases their postnatal follow-up is difficult because of their small size. These small kidneys are commonly misdiagnosed as renal agenesis.<sup>9,12</sup> Even with evident prenatal diagnosis, a postnatal work-up is needed to confirm the diagnosis and search for associated anomalies. A thorough clinical examination will complete the full fetal sonographic examination for other structural abnormalities, including heart, spine, extremities, face, and umbilical cord, as up to 35% may have extrarenal anomalies.<sup>13,14</sup> These are more likely to occur with bilateral than unilateral MCDK. Risks of chromosomal defects are low if there is isolated renal dysplasia.<sup>11</sup> Lazebnik et al<sup>13</sup> have found in a study of 102 cases with MCDK, 10 (9.8%) had an abnormal karyotype, but in all cases there were extrarenal anomalies present. Associated anomalies of kidneys contralateral to dysplastic kidneys are either structural (duplex system, pelviureteric obstruction, or ectopic) or affected by vesicoureteric reflux. The frequency of such anomalies is between 20 and 50%, according to published series.<sup>11,15–17</sup> Vesicoureteric reflux on the same side as the MCDK was reported in 17% of cases.<sup>18</sup>

Renal dysplasia frequently develops in conjunction with lower urinary tract malformation. Experimental urinary tract obstruction in animal models during development has generated dysplastic changes in renal structures.<sup>19,20</sup> The lower urinary tract should be assessed in cases of presumed renal dysplasia.

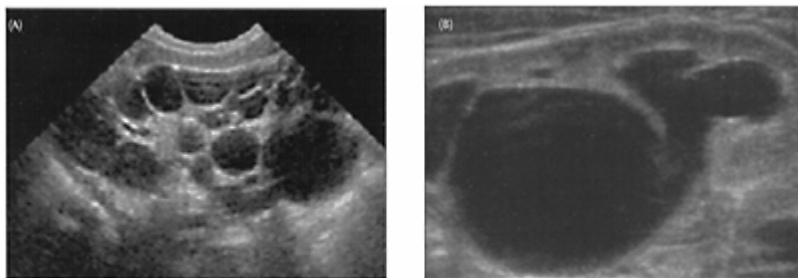
Our current postnatal work-up for prenatally detected MCDK includes a routine detailed ultrasound, voiding cystourethrography, and renal isotope scan. If the diagnosis is unclear, a Uro-MRI to differentiate MCDK from obstructive uropathy (Figure 59.2) or duplex system is performed.

### Natural history and prognosis of dysplastic kidneys

The prognosis of dysplastic kidneys depends mainly on whether the anomaly is unilateral or bilateral. Bilateral cases have poor prognosis and the fetus often has anhydramnios; death occurs in the neonatal period secondary to pulmonary hypoplasia. Other less severe forms of bilateral cases may survive the early childhood period and develop terminal renal failure later in life.<sup>11,16</sup>

The prognosis of patients with unilateral dysplasia with a normal contralateral kidney is much better. The majority of dysplastic kidneys involute<sup>9</sup> without causing any problems. The natural history is usually towards spontaneous regression of the cysts. Recently, Oliveira et al<sup>21</sup> found partial involution in 68%, complete involution in 21%, and an increase in unit size in 11%. The mean age at complete or partial involution of the lesion was 18 months. In unilateral cases, there is often a compensatory hypertrophy of the contralateral kidney.<sup>22</sup>

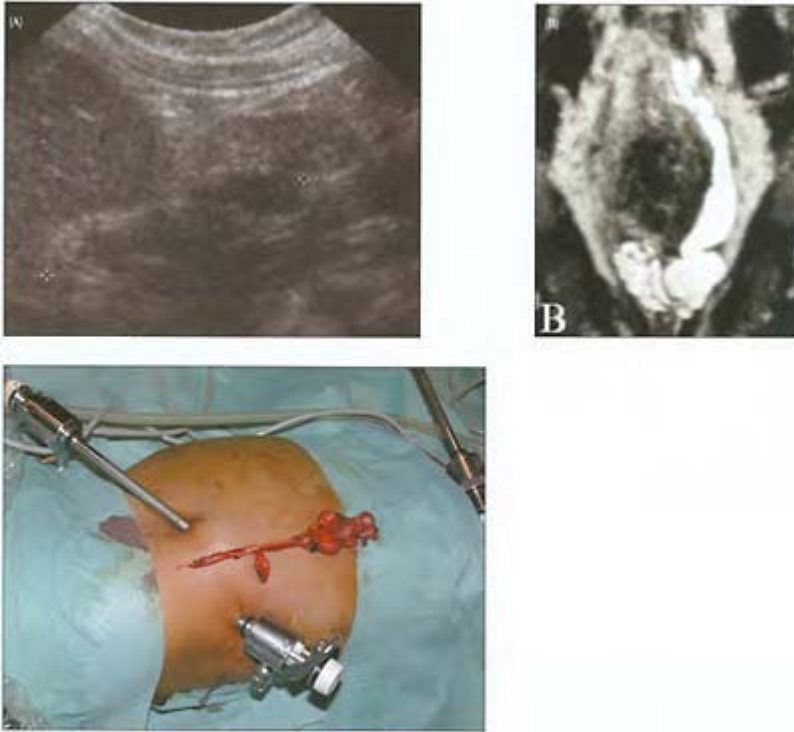
It was originally suggested that dysplastic kidneys be removed to avoid rare complications such as hypertension,



**Figure 59.1**

Sonographic diagnosis of multicystic dysplastic kidney (MCDK). Typical sonographic appearance of MCDK, a multiloculated retroperitoneal mass consisting of multiple thin-walled cysts, which do not appear to connect. To be differentiated from hydronephrosis (B), no renal pelvis or parenchyma can be demonstrated in MCDK (A). The cysts are distributed

randomly and the kidney is enlarged with irregular outline.



**Figure 59.2**

Magnetic resonance imaging (MRI) diagnosis of associated uropathy to a dysplastic nonfunctioning kidney. The sonographic appearance of an echogenic small nondifferentiated kidney (A). The MRI showed a small left kidney with ectopic implantation in the seminal vesicle (B). The anatomy of the entire left urinary tract can be detailed before surgery. The DMSA renal scan showed no function and a retroperitoneal left nephroureterectomy was done at 10 months of age (C).



tumors, and infections. However, the risk of these complications appears to be very low now that an elective nephrectomy is no longer routinely performed in most of centers. The likelihood of developing such complications is higher in cases associated with contralateral anomalies.<sup>17</sup> Patients with bilateral disease or associated genitourinary (GU) anomalies had a higher incidence of urinary tract infection (UTI) and progression to renal failure. Complex MCDK was associated with a worse outcome (50% chronic renal insufficiency or failure). Even the risk for chronic renal failure is very high: up to 22% with obstruction and 14% with contralateral reflux.<sup>22</sup>

Rare complications have been reported. Pain associated with MCDK was reported as the only symptom in older patients (mean age of 40 years old) with resolution after nephrectomy.<sup>23</sup> Exceptionally huge cysts may need percutaneous decompression to relieve the respiratory distress in infants.<sup>24</sup> Infection was suggested as a complication of MCDK, but any true association is not well documented. The reported cases were mostly associated with other urinary tract anomalies such as reflux or contralateral obstruction. In the registry of the American Academy of Pediatrics (AAP) for MCDK, 16 of the 608 nonoperated MCDK were associated with UTI.<sup>25</sup> Association between MCDK and hypertension was found in less than 1% in the published long-term series;<sup>25</sup> meanwhile, sporadic reports have demonstrated resolution of hypertension after nephrectomy.<sup>26</sup> Seeman et al<sup>27</sup> monitored blood pressure in children with unilateral MCDK and found anomalies only in children who had ultrasonographic and/or laboratory signs of contralateral kidney abnormalities.

There is ongoing controversy concerning the management of MCDK, particularly with regard to the potential for malignant transformation. Well-documented sporadic cases of malignancy with MCDK have been reported. The tumor may be Wilms' tumor, renal cell carcinoma, or mesothelioma.<sup>28,29</sup> Age is variable and can even be detected as early as 3 months. The discovery of the renal tumor on the initial ultrasound is more toward an association than the new development of tumor in the natural history of the disease. Even though this association or the malignant degeneration is exceptional, a careful initial ultrasound examination is mandatory and any equivocal diagnosis with suspicious nature of the cysts should lead to surgical removal of the kidney. These sporadic reported cases may lend support to the surgical management of MCDK, particularly as nephrectomy can now be performed in a day surgery setting with minimal morbidity.<sup>26</sup>

Few authors still advocate surgical removal of MCDK to avoid multiple and inadequate evaluations of those children with a single functioning renal unit.<sup>16,26</sup> Perez et al<sup>30</sup> have shown that early nephrectomy is more cost-effective than observation in neonates with MCDK only when observation involves screening with ultrasonography every 3 months until the child is 8 years old.

Controversy exists as to whether any screening program is necessary. When screening is instituted, options include monthly parental abdominal palpation vs serial renal ultrasound. The frequency is variable according to authors, between every 3 and 12 months until age 5–8 years old. The aim of this screening is dual: to screen for early stage tumors and to follow up contralateral renal growth.

### Management of solitary renal cyst

Other cystic diseases of the kidney are very uncommon in children. A single renal cyst is unusual, and even with otherwise normal-appearing kidneys, the diagnosis of PKD should always be suspected. Ultrasonography remains the modality primarily used for their evaluation. In general, computed tomography (CT) and magnetic resonance imaging (MRI) are limited to cases in which the ultrasonographic appearances are confusing or complications such as cyst rupture, hemorrhage, or neoplasia are suspected.<sup>31</sup> Once cystic lesions have been diagnosed by ultrasonography, a careful examination should rule out the group of cystic renal tumors that includes cystic Wilms' tumor and multilocular cystic nephroma. The multilocular cystic nephroma is a benign cystic tumor of the kidney occurring primarily in infant boys between 3 months and 4 years of age and in middle-aged women.<sup>32</sup> The tumor appears as a complex multicystic mass with thin septa separating the cysts.

The fetal simple renal cyst represents a distinct entity within the spectrum of cystic kidney disease. A fetal simple renal cyst can be identified by ultrasonography in early pregnancy.<sup>33</sup> In the absence of associated anatomic or chromosomal abnormalities, the majority of cysts will resolve during pregnancy without any sequelae.

Congenital calyceal cyst is another exceptional congenital anomaly that is also referred to as a calyceal diverticulum. The cysts are typically located more centrally adjacent to the collecting system. They may communicate with the collecting system and facilitate their diagnosis with the presence of contrast product in the cystic cavity on CT, but the communication may be stenotic and the diagnosis becomes less evident.<sup>34</sup>

Indications for surgical removal of solitary renal cysts in children are exceptional, as the natural history is spontaneous resolution and complicated cysts are seen more often in adults than in children. Laparoscopic unroofing of a solitary cyst in adults has been successful and is recommended in case of recurrence after percutaneous ultrasound-guided needle aspiration.<sup>7,35</sup> Few cases of cyst removal have been reported in children through a retroperitoneal laparoscopic approach. The access is the same as for nephrectomy and removal of the cyst can be achieved completely in a reasonable operative time not exceeding 1 hour.<sup>36,37</sup>

### Laparoscopic nephrectomy

The first laparoscopic nephrectomy in adults was reported in 1991 by Clayman et al.<sup>38</sup> One-year later Ehrlich et al.<sup>39</sup> reported their first series of pediatric cases. Since then many authors have reported successful results of nephrectomy and nephroureterectomy in pediatrics, all advocating the transperitoneal approach.<sup>40,41</sup> Roberts suggested the retroperitoneal approach to the kidney in 1976,<sup>42</sup> reporting his experience with retroperitoneal endoscopy with gas insufflation in animals. Retroperitoneal operative laparoscopy was described for the first time by Gaur in 1992<sup>43</sup> and then by others in adult and pediatric urology.<sup>44-46</sup> Despite the expanding application of retroperitoneal laparoscopic renal surgery in adults,<sup>47,48</sup> this technique was adapted later by pediatric

urologists and is progressively expanding in different centers.<sup>36,46,49–51</sup> We previously reported that the retroperitoneal approach is a well-adapted laparoscopic technique for renal surgery in children and is comparable to that of conventional renal surgery.<sup>36,52</sup>

Guilloneau et al<sup>45</sup> reported in a retrospective study of adults and children that retroperitoneal and transperitoneal approaches were equivalent in terms of morbidity and postoperative stay, but operating time was shorter with the retroperitoneal approach.

Effects of retroperitoneal CO<sub>2</sub> insufflation have been studied in animals and in children.<sup>52,53</sup> We have demonstrated a significant increase in systolic blood pressure and end-tidal carbon dioxide, while there was no modification of the other hemodynamic or ventilatory parameters. These changes do not need any special modification of the ventilatory parameters, whereas caution is required in hypertensive patients.

### *Indications and contraindications*

Currently, malignant renal tumors in children are not considered for laparoscopy. The most common renal tumor in children is nephroblastoma. These tumors are of large size, frequently extending outside the kidney, and with high risk of rupture during dissection. In adults, radical nephrectomy for renal cancer less than 5 cm in size can be safely achieved by a laparoscopic approach.<sup>47</sup>

Indications for nephrectomy in children are mainly for nonfunctioning kidneys secondary to obstructive uropathy or reflux. Although laparoscopic nephrectomy for MCDK is an easy and safe procedure, the indications for nephrectomy are still debatable. The acceptable indications for these cases are the increase in size of cysts or the rare complications of hypertension or infection.

Nephrectomy may be indicated for children with end-stage renal disease before transplantation when the primary renal disease is associated with hypertension, severe nephrotic syndrome, or severe uremic hemolytic syndrome.<sup>52</sup> In such cases, during open surgery, a large incision is necessary to control the renal pedicle in optimal conditions and to extract a large kidney, so here we find the ultimate advantage of laparoscopic procedures. Laparoscopic bilateral nephrectomy has been performed in adults.<sup>54</sup> In our experience, synchronous bilateral nephrectomy was performed in 10 children, and technically the procedure was performed as 2 unilateral cases, as position and draping were changed between the two procedures.

### *Patient and preoperative preparation*

The surgery is thoroughly explained to the child (adapted to his age) and to his parents. The possibility of conversion to open surgery has to be mentioned in the consent, along with the possible operative incidents.

Patient preparation is not different from the conventional surgery preparation. Personally we do not prescribe any specific diet measures before surgery. We follow the usual recommendations for general anesthesia preparations. The child is on a strict diet for a period between 4 and 8 hours, depending on his age, and premedicated before going to the operating theater. Some surgeons recommend a fluid diet and enema on the night preceding surgery.<sup>55</sup>

An indwelling bladder catheter is recommended in the case of high-grade reflux or each time that ureterectomy is indicated to facilitate the dissection of the ureter as close as possible to its junction with the bladder. Usually it is recommended in the transperitoneal approach to avoid bladder injury during trocar insertion. A preoperative catheter is also needed when urine output monitoring is mandatory for the anesthesia management in certain associated cardiac or renal diseases.

A nasogastric tube is placed after the endotracheal general anesthesia. Noninvasive hemodynamic and ventilatory monitoring is needed during the laparoscopic nephrectomy in either transperitoneal or retroperitoneal approach.

### *Recommended equipment and instruments*

Standard laparoscopic instruments are suitable for nephrectomy without special instruments or equipments. The usual laparoscopic equipment is necessary: monitor, insufflator, cold light source, and camera.

For any laparoscopic renal surgery, we recommend the following instruments.

### **Conventional surgical instruments for access**

1. Sterile marker to identify the major landmarks and optimal trocars placement.
2. Stab scalpel, No. 11, to achieve stab incision adapted for trocar insertion.
3. Blunt dissection scissors, helpful for muscle dissociation.
4. Needle driver.
5. Nontoothed forceps.
6. Nonresorbable monofilament suture with tapered needle for the purse-string suture.
7. Two artery forceps.
8. Pair of retractors, narrow and long blades.
9. Sutures necessary for wound closure.
10. Drains, at surgeon's convenience, with or without suction.
11. A complete conventional open surgery set, to be available in the operating room in case of conversion to open surgery.

### **Laparoscopic instruments**

The choice of single-use or reusable instruments depends usually on the surgeon's convenience and the economic impact. Currently, most of the instruments are available in the two categories. It is convenient to harmonize the type of instruments for all the surgeons and the different departments of surgery working together in the same operating theater. The laparoscopic instruments are the same for general pediatric surgery, and a common pool of instruments can be of great help, especially in the initial phase instruments, and for few unavailable instruments, we use during the learning curve. Personally, we mostly use reusable the single-use ones. Anyway, a full set of single-use instruments is necessary as back-up to reusable instruments:

1. Laparoscope: 5 mm 0° is the standard laparoscope for pediatric nephrectomy.

2. Trocars: 4 trocars of 5 mm; one of them should be blunt for the placement of the first trocar. Self-retaining trocars are interesting, especially in young children, to avoid the slipping of the trocars outside the abdominal wall.
3. Atraumatic grasping forceps.
4. Curved dissecting forceps for vascular dissection.
5. Scissors.
6. Monopolar diathermy.
7. Bipolar diathermy or harmonic scalpel.
8. Needle driver.
9. Toothed grasping forceps for organ retrieval.
10. Resorbable ligature for endocorporeal vascular or ureteral ligation when needed. A readymade laparoscopic loop suture can be used for ureteral ligation.
11. Resorbable suture, with round 3/8 curved needle, for transfixing ligature when needed or repair of vascular tear.
12. Vascular clips, reusable or single use.
13. Laparoscopic bag for organ retrieval; the currently available bags are at least 10 mm diameter and if the kidney is of big size, the first trocar and the laparoscope should be of 10 mm from the beginning to avoid trocar replacement at organ retrieval.
14. Irrigation-suction device.

### *Renal access*

The kidney can be accessed by a retroperitoneal or transperitoneal approach.

### **Retroperitoneal access**

**Lateral approach.** The patient is placed lateral, with sufficient flexion of the operating table so as to expose the area of trocars placement, between the last rib and the iliac crest (Figure 59.3). Retroperitoneal access is achieved



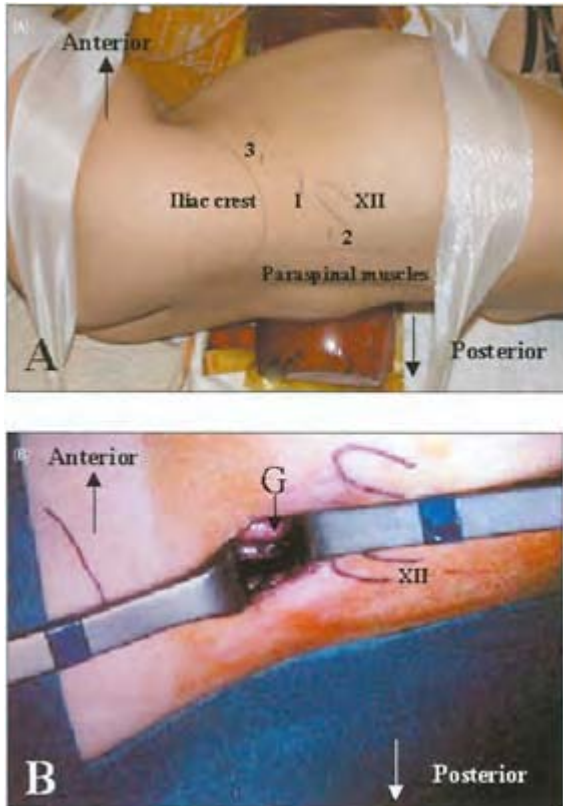
**Figure 59.3**

Patient positioning for left retroperitoneal laparoscopic nephrectomy. (A) The patient is placed

lateral, with sufficient flexion of the operating table so as to expose the area of trocars placement, between the last rib and the iliac crest; for younger children, as shown, a lumbar support is sufficient for the exposure. The child is wrapped by two adhesive bands, one on the greater trochanter level and a second on the chest, to keep the child at a perpendicular angle with the table. The surgeon, assistant, and scrub nurse are all on the back side of the child. The front side of the child is left free for the monitor, which is placed cranial while doing the kidney dissection and caudal to proceed for the distal ureterectomy. (B) Drapping is planned with fixation of all the connections with the monitor and insufflator towards the bottom and the head of the child leaving the exposed area free for instruments movement without difficulty.

through the first incision, 10–15 mm in length, and one fingerwidth from the lower border of the tip of the 12th rib (Figure 59.4). The use of narrow retractors with long blades allows a deep dissection with short incision. The Gerota's fascia is approached by a muscle-splitting blunt dissection; it is then opened under direct vision and the first blunt trocar (5 or 10 mm) is introduced directly inside the opened Gerota's fascia. A working space is created by gas insufflation dissection, and the first trocar is fixed with a purse-string suture that is applied around the deep fascia to ensure an airtight seal and to allow traction on the main trocar if needed to increase the working space. A second trocar (3 or 5 mm) is inserted posteriorly in front of the lumbosacral muscle. A third trocar (3 or 5 mm) is inserted in the anterior axillary line, a fingerwidth from the top of the iliac crest. To avoid transperitoneal insertion of this trocar, the working space is fully developed and the deep surface of the anterior wall muscles is identified before the trocar insertion. Insufflation pressure does not exceed 12 mmHg, and the CO<sub>2</sub> flow rate is progressively increased from 1 to 3 l/min. Access to the retroperitoneum and creation of the working space are the keys of success in the retroperitoneal renal surgery. Age is not a limiting factor for this approach. Young children have less fat and the access is easier; our youngest child was 6 weeks old.

**Prone posterior approach.** The access begins with an incision in the costovertebral angle at the edge of the paraspinal muscles. The secondary trocars are placed just above the iliac crest—one medially at the edge of the paraspinal muscles and one laterally at the posterior clavicular line.<sup>55</sup> In a randomized prospective study on 36 complete and 19 partial nephrectomies, Borzi<sup>56</sup> compared the lateral to the posterior retroperitoneal approach in children. There was no significant difference in the operative time. Our preference goes to the lateral approach: it permits any type of renal surgery at any age with good exposure to the distal ureter.



**Figure 59.4**

Trochars placement and retroperitoneal access for nephrectomy. (A) Area of trochars placement, between the last rib and the iliac crest. Retroperitoneal access is achieved through the first incision (1), 10–15 mm in length, and one fingerwidth from the lower border

of the tip of the 12th rib. A second trocar (2) is inserted posteriorly in the costovertebral angle. A third trocar (3) is inserted in the anterior axillary line, a fingerwidth from the top of the iliac crest. (B) The Gerota's fascia (G) is approached by a muscle-splitting blunt dissection; it is then opened under direct vision and the first blunt trocar is introduced directly inside the opened Gerota's fascia to start insufflation. The use of narrow retractors with long blades allows a deep dissection with short incision.

**Other techniques to access the retroperitoneal space.** Since the description by Gaur,<sup>43</sup> balloon dissection has been the method applied by most urologists. Disadvantages of balloon dissection are the cost of the disposable material and the possible complications with rupture of the balloon.<sup>57</sup> On the other hand, balloon dissection allows the creation of a working space without opening Gerota's fascia, which is important for radical nephrectomy of malignant tumors in adults.

Micali et al<sup>37</sup> reported the use of the Visiport visual trocar to access directly to the retroperitoneal space. The advantage of this method is the possibility of using a small incision for the first trocar, which is interesting in the reconstructive surgery but not in ablative surgery, as the first incision is needed for organ retrieval.

### **Transperitoneal access**

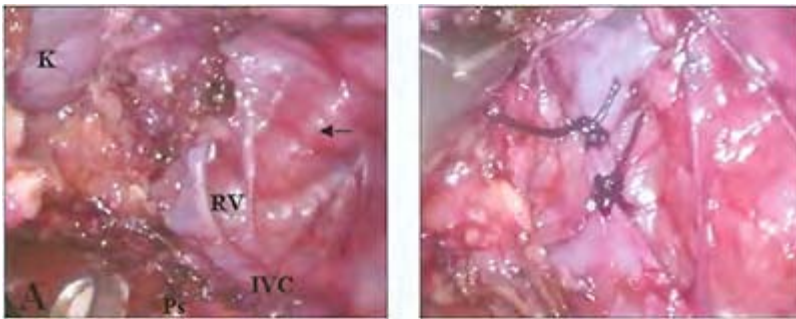
Several options exist in terms of patient positioning. The most frequently described is the flank position.<sup>55</sup> The pneumoperitoneum is created through an open umbilical approach. The child is positioned with the surgeon standing in front of the abdomen (opposite side of nephrectomy). The most frequent configuration has been with the umbilical port and two ipsilateral ports in the midclavicular line above and below the umbilicus. A fourth trocar may be placed in the midaxillary line for exposure to retract the liver or spleen if needed. The kidney is exposed by medial mobilization of the colon.

#### *Nephrectomy by lateral retroperitoneal approach*

The landmarks of the retroperitoneal space are first identified in order to be oriented with the retroperitoneal exposure. The psoas muscle is the posterior landmark and should remain in the bottom of the screen. The kidney remains attached anteriorly to the peritoneum, and should remain upward on the screen. The renal pedicle is identified and approached posteriorly (Figure 59.5), and dissected close to the junction with the aorta



and inferior vena cava (IVC), to avoid multiple ligations of branches of the renal vessels. On the left side, the vein is ligated distal to the genital and adrenal branches. On the right side, the vein is short and a careful dissection at its junction with the vena cava will avoid the confusion with dissecting the vena cava. After dissecting the renal artery then the vein, the vessels are clipped, ligated, or coagulated. The choice of method depends on the vessel diameter and the surgeon experience. In general, small arteries of MCDK can be coagulated by bipolar cautery, while the most common method is to double ligate the artery proximally by two clips and distally by one. The vein is generally clipped in the same way: if the diameter is bigger than the length of the clip, the vein is first ligated by resorbable intracorporeal knot, then clipped. The use of staples, as described in adult nephrectomy, requires a 12 mm port and is not needed in pediatric patients. The ureter is then identified and dissected as far as necessary. In the absence of reflux,



**Figure 59.5**

Retroperitoneal exposure and ligature of the renal pedicle. (A) The landmarks of the retroperitoneal space are first identified in order to be oriented with the retroperitoneal exposure. The psoas muscle (Ps) is the posterior landmark and should remain in the bottom of the screen. The kidney (K) remains attached anteriorly to the peritoneum, and should remain upward on the screen. The renal pedicle is identified and approached posteriorly. In this picture the artery is already ligated and sectioned and dissected close to the junction with the aorta and vena cava. On the right side, the renal vein (RV) is short and a careful dissection at its

junction with the inferior vena cava (IVC) will allow a safe exposure of its full length. Intestinal loops are visible behind the peritoneum and very close to the pedicle; monopolar cautery should be avoided in this area. (B) Ligature of the renal vein with intracorporeal knots.

the ureter is coagulated and sectioned at the level of the lumbar ureter (especially in pretransplant nephrectomy, the native ureter might be used for the transplantation). In the presence of reflux, the dissection is distally followed, the vas deferens is identified in males, and the ureter is ligated as close as possible to the ureterovesical junction. During this distal dissection, the surgeon moves towards the head of the child, and the screen goes towards the feet of the child. In the beginning of our experience, we were using a fourth trocar to dissect and ligate the distal ureter.<sup>36</sup> Currently, we use an endoloop or, if the ureter is large, a transparietal suture to fix the ureter to the abdominal wall to facilitate its distal dissection and ligation. As the peritoneum is very close to the ureter in this distal part, its dissection is left to the end of the procedure to avoid any peritoneal tear.

The last part of dissection is the anterior surface of the kidney. The kidney is dissected from the peritoneum very close to its capsule in the cleavage plane of areolar tissue. Usually no hemostasis is necessary in this plane, whereas, in inflammatory adherent kidneys, a sharp dissection with bipolar coagulation may be necessary. In the rare cases of xanthogranulomatous pyelonephritis, we perform the dissection of the adherent kidney through the subcapsular plane to avoid injury to intraperitoneal structures.

### *Kidney retrieval*

The kidney is usually retrieved through the initial incision (Figure 59.2). A 5 mm telescope is inserted through the accessory port, and a toothed grasping forceps is introduced through the 10 mm port to extract the kidney. The kidney is grasped at one of the poles, and pulled in this axis, to pull on its smallest diameter. In most cases, the kidney can be divided under vision during extraction through the muscle wall. In cases of severe pyelocalyceal dilatation or MCDK, direct evacuation by puncture helps in organ retrieval. An extraction bag is used for infected or large kidneys, and the kidney is morcellated inside the bag (Figure 59.6). Our current preference is for routinely using the bag for extraction to avoid extending the incision and the spillover of the parenchyma in the retroperitoneum, which might produce more postoperative inflammation. This is particularly important in the pretransplant group, where we have to minimize all the factors that might increase the postoperative retroperitoneal adhesions. In our experience these adhesions can render the vascular dissection during transplantation more difficult. If nephrectomy is associated to other lower urinary tract procedures, nephrectomy is performed first and the kidney is placed near to the bladder without transecting the ureter. Retrieval is carried out through the Pfannenstiel incision.

### *Postoperative care*

Postoperative care after transperitoneal laparoscopy is identical to any transperitoneal laparoscopic surgery in children.

The retroperitoneal nephrectomy does not require specific postoperative care. The nasogastric tube is removed at the end of the surgery. Analgesics are given according to the child's comfort and adapted pain scores. In few cases, especially after a difficult procedure or perioperative bleeding, postoperative ileus may develop, requiring special measures of gastric suction and fasting until the intestinal movements are reestablished. In the case of postoperative abdominal distention or discomfort, repeated abdominal examination is mandatory and completed by imaging if needed to exclude any intraperitoneal organ injury. Even in the retroperitoneal approach, the surgeon should keep in mind the possibility of such complications, especially if monopolar diathermy was used, with the possible injury of adjacent intraperitoneal organs.

### *Results*

In the exclusively pediatric laparoscopic nephrectomy series, results are consistent with the feasibility of the procedure and a very low rate of conversion to open surgery ranging from 0 to 3%.<sup>36,51,58-60</sup>



**Figure 59.6**

Kidney retrieval after retroperitoneal nephrectomy. The endobag is introduced through the first trocar and the kidney is placed inside the bag. Morcellation of the kidney by an artery forceps under direct vision allows kidney retrieval without the need to extend the incision.

The operative time is variable in the different series, according to the approach, indications, and the experience of the surgeon. In the retroperitoneal series, the mean operative time for nephrectomy or nephroureterectomy ranges from 47 to 110 min,<sup>36,51,56</sup> with longer time observed in the pretransplant group of children, with a mean operative time of 2 hours.<sup>52</sup> In the transperitoneal pediatric nephrectomy series, the mean operative time is relatively longer, at around 160 min.<sup>59,60</sup> As each group of take into consideration this difference of operative time as surgeons does one of the two approaches, it is difficult to comparison between the two approaches.

Pain and discomfort evaluation is a delicate procedure and should not be considered in nonrandomized series. To our knowledge, such a study on laparoscopic nephrectomy has yet to be published. The general impression of different authors is towards less consumption of analgesics, especially opiates, in the laparoscopic group. The shorter postoperative hospital stay may suggest that children are more comfortable and discharged earlier; here again, prudence is required in the analysis of retrospective nonrandomized series.

The hospital stay after laparoscopic nephrectomy depends on the indications. Most of the children operated on for urologic indications are discharged less than 24 hours after surgery.<sup>36,51,60</sup> Meanwhile, for pretransplant nephrectomy, the hospital stay is longer, with a mean of 4 days.

Although there is no comparative study on the cosmetic results of the treatments, it is obvious that the cosmetic results are excellent after laparoscopic nephrectomy, especially if the 3 or 5 mm trocar is used and the kidney retrieval is done through a laparoscopic bag when needed without extension of the incision.

### **Laparoscopic versus open nephrectomy**

To our knowledge, no prospective randomized study has proved the advantages of the laparoscopic approach over open surgery. We have retrospectively studied a comparable group of children who underwent pretransplant nephrectomy in our department before beginning our experience with retroperitoneal laparoscopic nephrectomy.<sup>52</sup> In this specific group of patients with end-stage renal disease, the hospital stay was significantly shorter after laparoscopic vs open nephrectomy (5.2 vs 8.4 days). Even when the operating time for laparoscopic vs open nephrectomy was longer (120 vs 104 minutes), the difference was not statistically significant. Hamilton et al<sup>58</sup> found comparable results on transperitoneal laparoscopic nephrectomy with significant decrease in hospital stay after laparoscopic compared with open nephrectomy (22.5 vs 41.3 hours). Operative time was significantly longer in the laparoscopic group (175.6 vs 120.2 min). Other studies on mixed groups of adults and children had comparable results, with a significantly briefer postoperative course in the laparoscopic group.<sup>61</sup>

### **Common and unusual intraoperative problems and how to identify them**

Complications of abdominal laparoscopy for urologic procedures, such as bowel and great vessel injury, have been documented in the adult and pediatric populations.<sup>62-64</sup> In a multicentered survey of 5400 pediatric urologic laparoscopic procedures, Peters<sup>62</sup> showed that the clearest predictor of complication rate was laparoscopic experience. Soulie et al<sup>64</sup> have reported a decrease of complication rate from 9% for the first 100 to 4% for the subsequent 250 procedures. Most intraoperative complications (2.6%) were vascular and visceral injuries, whereas postoperative complications (2.8%) were predominantly thromboembolism and wound infection at trocar sites. Complications of retroperitoneal renal surgery are rare and mainly vascular or colonic injury. Kumar et al<sup>65</sup> reported a major complication rate of 3.5% of 316 patients (aged 4–88 years) who underwent retroperitoneoscopic urologic surgery. Vascular injuries occurred in 7 patients, 5 of whom required immediate conversion to open surgery. Four patients (1.2%) had other major complications, including colonic injury, retroperitoneal collections, and incisional hernia.

In our experience with 65 retroperitoneal nephrectomy cases, we had one vascular tear, during a teaching session, at the origin of a lumbar vein, in a case of xanthogranulomatous pyelonephritis. A clip without the need to convert to open surgery successfully closed the tear. In retroperitoneal procedures, traction on the kidney towards the top of the screen stretches renal vessels, reducing bleeding while evaluating the feasibility of the hemostasis by laparoscopic measures. The only postoperative complication we experienced was a postoperative hematoma after pretransplant bilateral nephrectomy; this hematoma was drained percutaneously. In the pretransplant kidney, we recommend an indwelling drainage tube for 24 hours.

The most common incident of the retroperitoneal approach is the pneumoperitoneum secondary to peritoneal tear.<sup>36,65</sup> This incident occurred in nearly 30% of our cases in the early experience, but then could be avoided by careful preparation of the retroperitoneal space for insertion of the anterior working ports. When this occurs at the beginning of the procedure, the retroperitoneal working space is reduced by the effect of the pneumoperitoneum. This can be managed either by laparoscopic suturing of the tear or, if this is not possible, by inserting a Veress needle in the peritoneal cavity to evacuate the gas during the procedure. If the tear occurs after the ligature of the renal vessels, during dissection of the anterior surface of the kidney or the ureter, the procedure can usually be accomplished without special management of the pneumoperitoneum.

### **Conclusion**

Minimally invasive procedures emphasize our goals of improving patient comfort and safety while adapting the laparoscopic procedures as closely as possible to conventional surgical techniques with respect to the operative time, cost, and surgical principles.

Indications of laparoscopy in pediatric urology are expanding with more centers being involved in the evolution of the different procedures. To avoid a discouraging learning curve, we recommend pediatric urologists acquire their experience in a progressive pattern. Nephrectomy for MCDK or hydronephrosis is a relatively safe and easy procedure for getting the surgeon to use the laparoscopic exposure of the upper tract. When the surgeon is familiar with the exposure, he can proceed to more difficult nephrectomies: pretransplant and partial nephrectomy.

Time can only be limited by training. Today, training is easily available in many centers of adult and pediatric surgery. Experienced peers are also available to accompany the surgeon in his initial experience, especially in the era of telerobotic surgery.<sup>66</sup> Mentored laparoscopic teaching is a safe way to introduce advanced urologic laparoscopic procedures in the pediatric urology department.<sup>67</sup> This might improve the results of the surgeon's initial experience with laparoscopy and encourage its development among a larger number of pediatric urologists.

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## Pediatric lower urinary tract minimally invasive surgery

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### Endoscopic management of reflux

The least invasive procedures for the treatment of vesicoureteral reflux require no incision at all. In the early 1970s, Teflon (polytetrafluoroethylene paste) was first cystoscopically injected into the bladder neck to treat urinary incontinence. Matouschek introduced the idea of Teflon injection to treat reflux in 1981.<sup>1</sup> The subureteric injection was popularized by O'Donnell and Puri in the early 1980s and termed the STING procedure.<sup>2</sup> Since that time, multiple injectable substances have been developed and studied in order to provide the ideal treatment for reflux. This ideal substance should be nonimmunogenic, nonmigratory, noninflammatory, stable over time, and deliverable via a cystoscope. Although the injectable substances vary, the technique is essentially the same for all subureteric injection procedures.

The procedure usually lasts about 15 min and is performed under general anesthesia via the cystoscope. A needle perforates the mucosa 3–4 mm distal to the ureteral orifice at the 6 o'clock position. The needle is then advanced 5–8 mm prior to injection, with the targeted space being the lamina propria. The needle is left in place for about 30 s after injection to prevent extrusion after needle removal. Visually, the final goal of injection is an inverted crescent shape to the ureteral orifice. Ureteral catheterization may be used to facilitate the injection, and either the lower pole ureteral orifice or both may be injected for duplicated systems. Results have varied using this same technique with different substances, and most debate regarding endoscopic treatment of reflux deals with the specific safety profile and efficacy of those substances.

### *Teflon*

Subureteric Teflon injection or STING is the oldest of these procedures and hence has the longest follow-up to date. Teflon consists of polytetrafluoroethylene (PTFE) particles in a 50% suspension with glycerine. After injection, the glycerine is absorbed, leaving the PTFE particles in place permanently. A fibrous capsule then forms around the Teflon plug. The STING procedure has been mainly performed in Europe. With 11–17 years of follow-up reported in one series by Chertin et al, 393 ureters in 258 patients were injected with Teflon, with a mean follow-up of 13.5 years.<sup>3</sup> Preoperatively, reflux was graded as follows: grade II 4.1%, grade III 64%, grade IV 25%, and grade V 7%. Reflux resolved

after one injection in 76.8% and converted to grade I or II in 4.8%, requiring no further treatment. A cumulative success rate of 90.3% was achieved after a second injection, 92.9% after a third, and 93.4% after a fourth. Open ureteroneocystotomy was required in 1.8% of ureters that were refractory to STING treatment. No adverse effects related to the Teflon were noted, and there was no particular difficulty with the post-STING reimplants. A 5% long-term recurrence was described, and these patients were observed for low-grade reflux and subjected to a repeat procedure.

A large, multicenter European survey yielded similar results to the Dublin data:<sup>4</sup> 53 pediatric surgeons in 41 centers responded to the survey and were able to amass a STING database of 12,251 ureters in 8332 children with a median follow-up of 6 years; 75.3% and 87.4% ureteral resolution rates were seen after one and two injections, respectively. Open ureteral reimplantation was required in 4.5% because of failed STING and in 0.33% because of post-STING obstruction. The STING procedure has also been shown to have slightly poorer results for STING after failed reimplant and in duplex systems.<sup>5-7</sup>

The main concern that has arisen since the introduction of STING has been the safety profile of injecting a nonbiologic substance into children. Aaronson et al showed the ability of Teflon to migrate to the lungs and brains in dogs who had their bladders injected.<sup>8</sup> Three cases of Teflon migration to pelvic lymph nodes in post-STING children have also been reported.<sup>9</sup> Most concerning is a case of ischemic brain injury that occurred in a 6-year-old girl 1 year after STING, although her stroke could not be definitively linked to Teflon migration. Because of the concerns of Teflon migration, the STING procedure has gained limited acceptance in the United States. However, proponents of the procedure note that no adverse effect of Teflon migration has been noted in their large series of patients with extended follow-up.

### *Collagen*

Bovine collagen has also been investigated as a biologic alternative to Teflon. Bovine collagen is treated with pepsin to decrease antigenicity and cross-linked with glutaraldehyde (a combination termed GAX) to prevent breakdown. After injection, histology reveals a foreign body reaction with fibroblast invasion and human collagen.<sup>10</sup> Although collagen is a biologic substance which inherently seems safe, there are immunologic concerns with injection of bovine collagen. All candidates should be skin tested 4 weeks prior to the procedure. Three percent will demonstrate a delayed hypersensitivity reaction and are not eligible for the procedure termed SCIN (subureteric collagen injection). After injection, 22–30% will develop antibovine collagen antibodies, predominantly immunoglobulin G (IgG) type.<sup>11,12</sup> There have been no documented cases of autoimmune disorders with SCIN, although this remains a concern and theoretical possibility. The only known immunologic complication in pediatric patients is a local inflammatory reaction after repeat injection in a seropositive girl.<sup>12</sup>

Even with these immunologic possibilities, the greatest obstacle to widespread SCIN is its lower resolution rates and lack of long-term durability. Frey et al performed SCIN in 132 patients and 204 ureters.<sup>13</sup> At a median follow-up of 33 months, reflux resolved in 62.7% of ureters after a single injection and 66 ureters underwent a second injection with a 54.5% resolution rate; furthermore, 10% developed a late recurrence of reflux. The tendency of reflux to recur late in collagen injection patients was marked in another study

of 58 refluxing ureters in 36 patients.<sup>14</sup> Initial reflux resolution was 95%, but declined to 35% at 1 year and only 9% after 37 months. The explanation for the long-term failure of collagen injections is bovine collagen breakdown and volume loss of the subureteral plug. The collagen preparation used routinely has a final collagen concentration of 35 mg/ml (GAX 35), and has been shown in a pig model to decrease its size by 27% at 6 months after injection. A 65 mg/ml paste (GAX 65) has been developed to prevent breakdown and, in the same porcine model, implant volume decreased by only 0.1%.<sup>15</sup> GAX 65 injections were performed in 28 ureters with a 3-month resolution rate of 87.5%.<sup>16</sup> However, long-term studies have not been published and cannot address the biggest concern of SCIN, which is the question of long-term durability.

### *Polydimethylsiloxane (Macroplastique)*

Polydimethylsiloxane is a solid, silicone elastomer that has also been investigated as an injectable substance. Macroplastique consists of these particles suspended in a hydrogel with a mean particle size of 209  $\mu\text{m}$ .<sup>17</sup> The larger particle size provides a theoretical advantage to limiting migration of the material, since macrophages are unable to phagocytose particles greater than 80  $\mu\text{m}$ . Histologically, a fibrous capsule develops around the implant, surrounding a foreign body reaction. Clinical results reveal 81% overall reflux resolution rate after a single injection and 18 months median follow-up.<sup>18</sup> This rate increased to 90% after two injections. Interestingly, resolution rates declined as reflux grade increased, with a major decrease in efficacy for grade IV reflux (45% resolution). In children with bilateral reflux, patient resolution rates decreased to 74% after one injection and 87% after two. Long-term recurrent and de-novo reflux developed in 3% and 3% of patients, respectively. Other clinical series have similar resolution rates in a similar short follow-up period.<sup>19</sup>

In much the same way Teflon is viewed, polydimethylsiloxane has considerable clinical success but also raises concerns of patient safety. Smith et al demonstrated particle migration locally and distantly to the spleen in dogs after subureteral injection.<sup>20</sup> Periurethral injections in another dog study revealed migration to a lung venule. Lymph node migration after subureteral injection in a 10-month-old girl has also been reported.<sup>21</sup> These findings, coupled with a troubled past of silicone implants in the United States, no doubt will be a formidable obstacle to the widespread use of Macroplastique in the United States despite its relative clinical efficacy.

### *Deflux*

Because it consists of a biologic material with a theoretically better safety profile, Deflux has received greater recent attention and enthusiasm in the United States. The injectable paste consists of 80–120  $\mu\text{m}$  microspheres of dextranomer (a polysaccharide of dextran) suspended in hyaluronic acid. Because of its relatively larger size, Deflux is theoretically less likely to migrate beyond the subureteral space. In a rabbit model, the dextranomer spheres did not demonstrate migration to other organs.<sup>22</sup> Even if Deflux were to migrate, it would probably be hydrolyzed to glucose and water. After implantation, histologic findings of the distal ureter reveal granulomatous inflammation with multinucleated giant cells and other inflammatory cells. The implant site is surrounded by a fibrotic pseudo-

capsule containing dextranomer at different stages of resorption and calcification as well as eosinophils in some patients but not others.<sup>23</sup>

The demonstration of dextranomer resorption in vivo raises the question of long-term durability. However, relatively long-term follow-up is available after Deflux injection. A retrospective review of 221 patients with 334 refluxing ureters was performed with a mean follow-up of 5 years.<sup>24</sup> Overall, 68% of patients and 75% of ureters had a positive response (grade I or less) at time of last follow-up. Only 54% of patients demonstrated grade I or less reflux after a single injection. A 4% long-term recurrence rate was also demonstrated. No obstruction or hydronephrosis developed as well. As with other materials, resolution rates tended to be higher for lower grades of reflux. Other studies with shorter follow-up times reveal only slightly better results.<sup>25,26</sup>

Based on the above clinical results, a computer model was developed to compare cost of traditional reflux management to different clinical scenarios that included endoscopic injection with Deflux. Although methodology of the study may be questioned, it does point out the potential savings in the overall cost of correcting reflux when using subureteric injection approaches, with savings ranging from \$889 to \$2218 per patient, depending upon the clinical scenario.<sup>27</sup>

#### *Other materials and issues*

In addition to the injectable substances used most commonly, other materials are being investigated currently. Urocol paste consists of triple calcium phosphate ceramic suspended in a gel. At 6 months follow-up, 71% success has been reported in 346 ureters.<sup>28</sup> Coaptite is a similar calcium hydroxylapatite suspension that has been used in 40 patients. Initial 3-month cure rates for grade II, III, and IV were 95%, 55%, and 42%, respectively.<sup>29</sup> Autologous chondrocytes have also been injected. They have the advantage of avoiding concerns about foreign materials but do require a second anesthetic to harvest the chondrocytes. Results at 3 months show a 57% success rate for a single injection. At 1 year after multiple injections, 70% of ureters and 65% of patients are cured.<sup>30</sup> All of these newer materials lack long-term follow-up, but may prove to be comparably better substances.

Another issue that has been raised by Capozza et al has been the use of endoscopic injection in children with voiding dysfunction. They hypothesize that high voiding pressures cause displacement of the implant material and are responsible for many treatment failures. Based on voiding dysfunction questionnaires, they have shown that success rates decline as the degree of voiding dysfunction increases. The authors have concluded that endoscopic injection should not be performed in untreated dysfunctional voiders.<sup>31</sup>

#### *Summary*

The combination of antibiotic prophylaxis and open surgical ureteral reimplantation has had great success in the management of vesicoureteral reflux. Many children, especially with low-grade reflux, can be spared any manipulation with prophylaxis as their reflux resolves naturally with time. Open reimplantation has a remarkable success rate, with relatively rare complications and minimal morbidity. Most children are discharged from

the hospital in 1 to 2 days with low pain medication requirements. Certainly, the bar is high for other management techniques. Even with these successes, we should still continue to find ways to improve and limit the discomfort that our treatment strategies have on our young patients. Current goals include decreasing hospital stay, limiting cystography, minimizing pain, and lowering costs of treatment. Endoscopic management holds great promise because it may accomplish many of these goals. However, questions as to the long-term stability and safety of the procedure remain. Injections of Teflon and silicone particles have the highest resolution rates and seem to be more durable, but particles have been shown to migrate in children. Many physicians have a great sense of unease about implanting a foreign material that will remain with the child for a lifetime. Alternatively, biologic materials have been employed, but are hampered with durability issues as the body breaks down the implant over time. Studies on collagen injections have clearly shown that long-term recurrence is an obstacle to its widespread use. Deflux appears to maintain its implant volume for longer periods of time, but histologic studies show that the material is resorbed from the implant site, although at a lesser rate than bovine collagen. At the current time, Deflux has a growing number of proponents. Surgeons are willing to accept the lower success rates for a greater safety profile. The reflux resolution rates can also be maximized by applying the procedure to select patients: namely, those with lesser grades who lack voiding dysfunction.

In its current state, endoscopic management is seen as a substitute or alternative to open reimplantation. However, because of its minimally morbid nature, subureteral injection may alter the way we approach reflux completely. This technique could easily be applied in early treatment as an alternative to antibiotic prophylaxis. One study has already demonstrated higher resolution rates with Deflux when prospectively compared to antibiotic prophylaxis in short follow-up. More research on the application of current materials as well as the development of new materials is warranted.

### **Origins of percutaneous bladder procedures**

The smaller bony structure of the pelvis in children causes the bladder to assume an intra-abdominal position. This creates relatively easy access to this area for minimally invasive procedures. For decades, suprapubic access to the bladder for urine aspiration and culture has been a standard practice in young children. As instrumentation has improved, a variety of problems have been approached in this manner, including things such as antegrade ablation of posterior urethral valves via a trocar placed into the bladder.<sup>32</sup> More recently, it has been suggested that placing a scope through such an access port may be of value in observing the bladder neck while periurethral injection of bulking agents is performed. Additionally, suprapubic access is valuable as an adjunct to ureteroscopy or ureteral catheterization in patients with an altered ureteral positioning, such as those having undergone cross-trigonal reimplants<sup>33</sup> or renal transplantation where transurethral approaches may fail. Experience with occasional transvesical procedures such as these inevitably led pediatric urologists to apply these techniques to the correction of the common problem of vesicoureteral reflux.

*Extravesical ureteral reimplantation*

Initial attempts at laparoscopic correction of reflux were made transperitoneally using a modified Lich reimplant technique.<sup>34</sup> The techniques were initially reported in 1993–94 in a porcine model.<sup>35,36</sup> Since vesicoureteral reflux does not naturally occur in most animals, the reflux had to be first created by making an endoscopic incision of the ureteral tunnel. One camera port and two or three other transperitoneal working ports were utilized and the posterior bladder wall was exposed. Detrusor incisions were made superolateral to the ureteral hiatus, detrusor muscle was separated from the epithelium, the ureter was positioned within the trough, and the detrusor was closed over the ureter with absorbable sutures or staples. In these studies, 13–15 laparoscopic reimplanted ureters were free of reflux at 3–6 months after surgery, while one ureter became obstructed. The average operating times were 132 and 141 min in the two respective studies.<sup>35,36</sup>

In 1994, Ehrlich et al reported on two patients with successful outcomes from laparoscopic extravesical reimplantation.<sup>37</sup> Shortly after, Janetschek and coworkers reported outcomes in 6 children,<sup>38</sup> one of whom required postoperative ureteral stenting for 6 weeks. The authors felt that the procedure was complex and unwieldy and offered no significant advantage to the patients. Despite this, others have pursued extravesical laparoscopic reimplantation in children. Fung and colleagues have more recently reported 36 ureters repaired in 26 children (ages 4–13 years old).<sup>39</sup> Their technique involved utilizing four ports; only one patient had persistent reflux at 3 months and the operative time was about 1.5 hours per ureter. Even with improved techniques, the overall recovery from a laparoscopic extravesical reimplant seems to be not significantly easier or quicker than that following open extravesical reimplant procedures, except possibly in the amount of pain medicine required. Because of the difficulty in fully visualizing the deep retrovesical space and the steep procedural learning curve involved, this technique has not gained widespread acceptance.

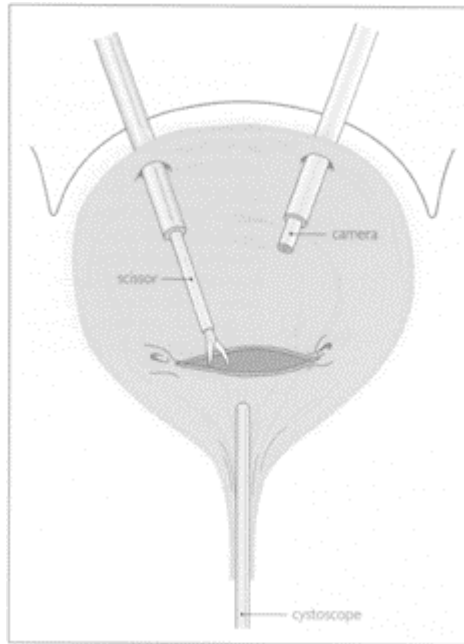
*Transvesical ureteral reimplantation*

Following the initial reports of laparoscopic extravesical reimplantation, two groups reported on experience with combined laparoscopic (transvesical) and cystoscopic (transurethral) reimplantation in adults and children.<sup>40,41</sup> These procedures were initially based upon the Gil-Vernet trigonoplasty technique<sup>42</sup> and have been termed endoscopic trigonoplasty or percutaneous endoscopic trigonoplasty (PET procedure).

The technique of the combined transvesical/transurethral approach to reimplantation begins with cystoscopy to assess the bladder. Two small transvesical trocars are placed under cystoscopic guidance at the 10 and 2 o'clock positions near the dome of the bladder (Figure 60.1). An Endoclose needle (Ethicon) is used to pass a 2–0 polyglactin suture just beside the trocar through the rectus fascia and muscle and into the bladder. A cystoscopic grasper retrieves the free end of the suture within the bladder and the empty needle is withdrawn and passed again on the opposite side of the trocar. The grasper then passes the suture to the empty Endoclose needle and the suture is drawn up through the fascia to the skin (Figure 60.2). The suture is tied loosely around the trocar and prevents

the bladder wall from slipping off of the trocar during the procedure. The same is done for each trocar placed into the bladder. This placement technique will allow for single suture closure of the bladder wall and rectus fascia and muscle.

The bladder is then drained and 'pneumobladder' is created with CO<sub>2</sub> insufflation. The cystoscope may be used



**Figure 60.1**

Two transvesical trocars are placed under direct cystoscopic guidance at the 10 and 2 o'clock position near the dome of the bladder (12 o'clock position).

for suction of the operative site or, with the grasper inserted, for retraction during the procedure. During endoscopic trigonoplasty, the bladder epithelium between the two ureteral orifices, along the interureteric ridge, is cauterized and then using the miniature laparoscopic scissors the bladder epithelium is elevated both on the superior and inferior edges to create a 1 cm wide trough (Figure 60.3). Then, 3–0 polyglactin sutures (2) are placed on the medial edge of each ureteral orifice in such a fashion as to bury the knot when the suture is tied (Figure 60.4). This draws the ureteral orifices to the midline over exposed bladder muscle (Figure 60.5). Interrupted 4–0 polyglactin sutures are then used to reappose the bladder epithelium in the midline and complete the reimplant. Catheter drainage is used postoperatively, leaving either a small tube via a trocar site as a

suprapubic tube or placing a urethral catheter. The trocars are removed and the sutures tied, which creates a watertight bladder wall closure and closes the fascia at the same time.

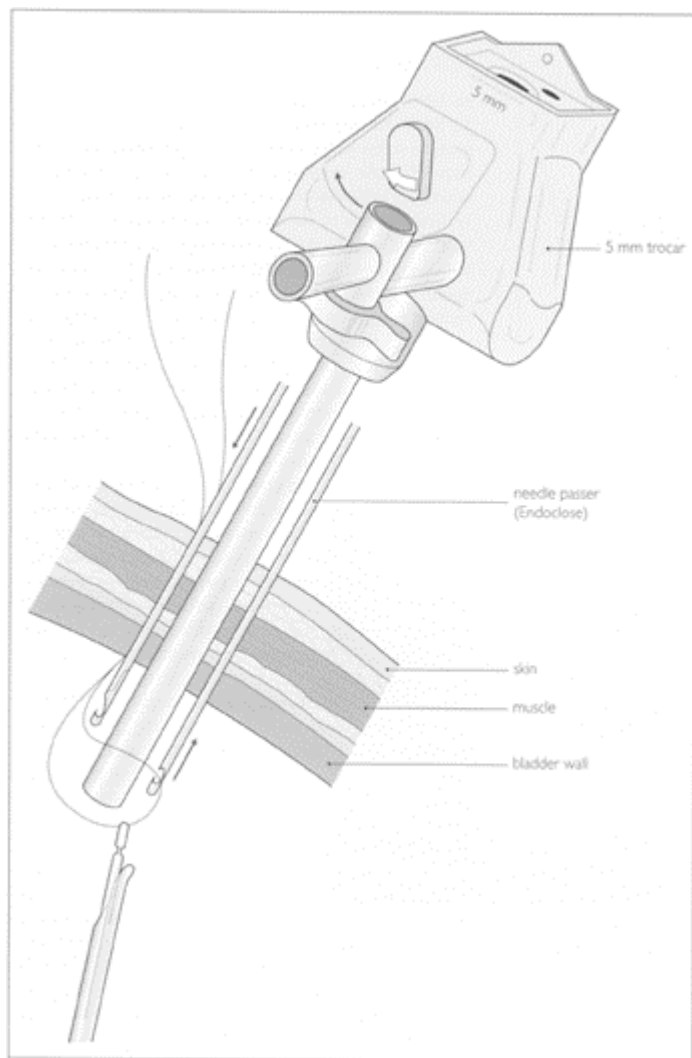
### *Combined endoscopic/transvesical reimplant results*

In 1995, Okamura and associates reported outcomes in 12 adult patients with low- and moderate-grade vesicoureteral reflux utilizing the endoscopic trigonoplasty technique.<sup>40</sup> Their technique differed slightly from the one described with the two suprapubic trocars placed in the vertical midline of the bladder and suturing being done with a 'ski' needle via the cystoscopic grasper rather than with a needle holder placed through a port. A single horizontal mattress suture was used and early cystogram showed resolution in all patients. In 1996, Cartwright et al reported their experience of 22 children having the percutaneous endoscopic trigonoplasty procedure.<sup>41</sup> Reflux was of a moderate grade in most and a high grade in a few. There was no ureteral obstruction encountered and no reflux immediately after the procedure. As follow-up was extended to 6 months, reflux resolved in 20 of the 32 ureters, for a resolution rate of 62.5%. Success could not be correlated to patient age, laterality, initial grade of reflux, or preoperative bladder instability. Complications were encountered, including significant hyponatremia and a perivesical urine collection requiring drainage. It was the authors' opinion that this was technically feasible but the learning curve was significant and technical modifications were necessary to improve the modest success rate to an acceptable level.

Pursuing the transvesical laparoscopic reimplant one step further, Gatti et al modified the procedure by completely mobilizing the ureters.<sup>43</sup> Trocar placements were similar and a stent was placed within the ureteral orifice and sewn to mucosa. Using the cystoscopic graspers, the orifice could be retracted, aiding greatly in the dissection. Using the miniature laparoscopic scissors, 2.5 cm of ureteral mobility was obtained; there was a technical concern that further dissection extravesically would allow CO<sub>2</sub> to escape in large amounts into the retroperitoneum, causing collapse of the working space within the lumen of the bladder. Tunnels for reimplanting the ureters were created by incising and dissecting the mucosa to create an appropriate cross-trigonal orientation. The dissected muscular hiatus was closed and the ureters were drawn across the bladder and secured with polyglactin sutures and epithelium closed over them. Subepithelial tunnel lengths of 2–2.5 cm were obtained. At 1 year follow-up, 10 of the 12 ureters showed no vesicoureteral reflux (5 of 7 patients). Yeung and Borzi have also performed cross-trigonal reimplants in 4 patients with good results.<sup>44</sup>

In 1997, Okumura and associates published a study with follow-up on 28 patients, many of whom were children who had undergone their endoscopic trigonoplasty.<sup>45</sup> Their resolution rates at 1–3 months were 95%, which had





**Figure 60.2**

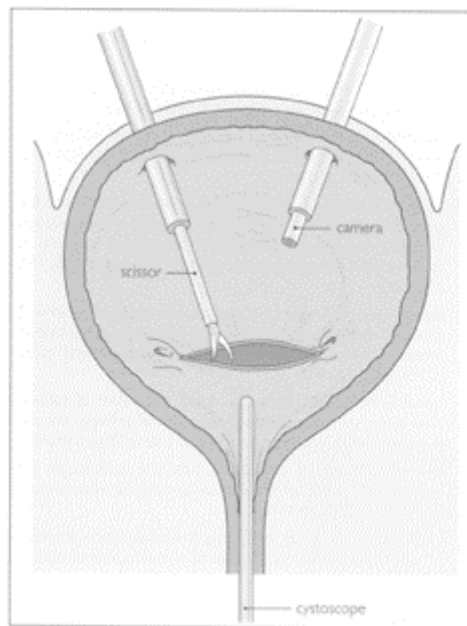
Prevent the bladder wall from slipping off of the canulla by passing a 2–0 polyglactin suture alongside the trocar through the rectus fascia and muscle and into the bladder. The suture is grasped and withdrawn on the opposite side of the trocar. The suture is tied loosely around the trocar insufflations

side arm. This is repeated with the other transvesical trocar. This same suture is utilized to close the bladder wall and rectus fascia at the conclusion of the procedure.

decreased to 79% at 12 months. As Okumura et al did cystoscopy to evaluate their surgical repair, they found that the trigone had split in 5 of their patients, resulting in recurrent reflux in 3 patients. This same group continues to work on technique alterations to improve the outcome, being convinced that the recovery is better than that in open reimplant surgery (especially in adults).<sup>46-48</sup>

### *Bladder autoaugmentation*

Another minimally invasive operation that has been performed on the bladder is bladder autoaugmentation or detrusor myectomy. This has generally been carried out transperitoneally, exposing the dome of the bladder and taking great care to dissect away detrusor fibers while



**Figure 60.3**

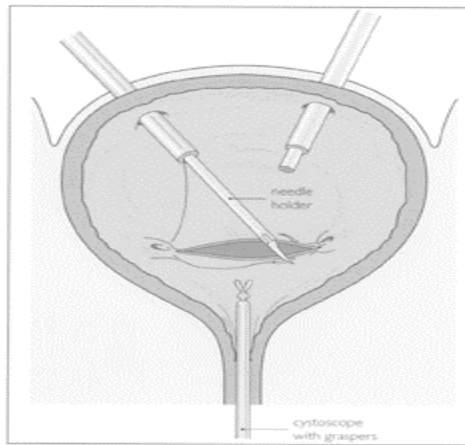
During endoscopic trigonoplasty, the bladder epithelium between the two ureteral orifices is incised with

electrocautery, along the interureteric ridge. The trough is developed by elevating the superior and inferior edges with mini-laparoscopic scissors to create a 1 cm wide trough.

keeping the epithelium intact and using either cautery or laser to divide the fibers. This allows the bladder epithelium to bulge into the peritoneal cavity, creating a bladder diverticulum at the dome in hopes of lessening filling pressures, minimizing detrusor instability, and (at times) to increase bladder capacity.<sup>49,50</sup> In general, results of laparoscopic autoaugmentation mirror those of open surgery.

### *Miscellaneous procedures*

There are unusual circumstances in which minimally invasive techniques may be creatively applied. One of the authors laparoscopically repaired an injury to the bladder neck and urethra discovered during laparoscopic partial colectomy and pull through (with mucosal proctectomy) in a 1-month-old baby. Placement of a transvesical trocar, in addition to the peritoneal trocars, allowed for guiding the difficult placement of a catheter across the injured area. In addition, laparoscopy has been used by the authors to close isolated bladder dome rupture from trauma.



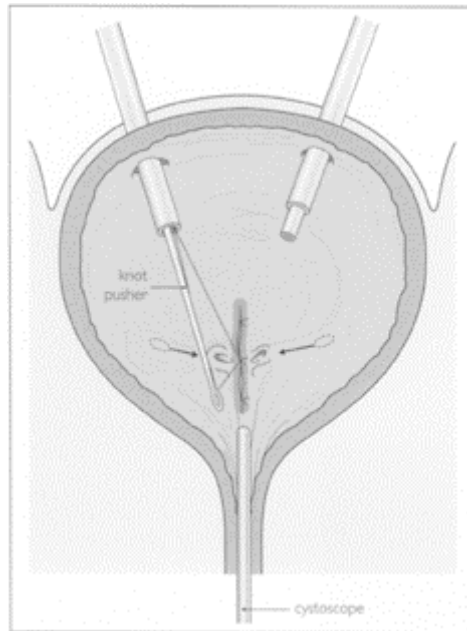
**Figure 60.4**

Utilizing mini-laparoscopic needle drivers, a 3-0 polyglactin suture (2) is placed on the medial edge of each ureteral orifice in such a fashion as to bury the knot.

### Perspective

Laparoscopic surgery in children carries the significant benefit of improved cosmesis, creating only small trocar site scars. However, the benefit of rapid recovery and return to full activity, which is well documented in the adult literature, is less well defined or demonstrable in this group. Younger children often bounce back so promptly from modest open procedures that the room for improvement in this regard is smaller than in adults. Indeed, in our practice, we will often perform unilateral, extravesical open reimplant as an outpatient procedure in younger children.

This said, as more precise and pediatric-specific laparoscopic equipment is designed, there is reason to think that our current techniques will be improved. In addition, the development of staples and clips that do not become the nidus for stone formation in the urinary tract would be of great utility. The current and mounting experience with robotic laparoscopic systems seems to hold great promise for the precise reconstructive ability required for good



**Figure 60.5**

After placing and tying the suture, both ureteral orifices will be drawn closer to the midline.

outcomes in children. It appears clear that minimally invasive approaches to bladder surgery in children will continue to be pursued and will probably become, with time and experience, common surgical approaches.

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## Pediatric voiding dysfunction, neurogenic bladder, and posterior urethral valves

Victor Braren

### Introduction

The lower urinary tract in children has long been approached using minimally invasive treatment techniques. The challenges of posterior urethral valves (PUV) and abnormalities of the bladder neck were well suited to these methods of management. Endoscopic approaches to lower urinary tract anatomy have required pediatric urologists to adapt miniaturized equipment and fine tune techniques for treatment of anomalies of this area. This has even allowed treatment of newborns.

As is so often the case, terminology becomes a problem in dealing with the lower urinary tract. Unacceptable, oxymoronic neologisms and misnomers such as ‘non-neurogenic neurogenic bladder’ have unfortunately made their way into the literature. Even the term ‘voiding dysfunction’ has been criticized as covering only a part of the impairment spectrum, disregarding the storage and other lower tract functions that may become deranged. However, if one assumes that storage must occur in order for voiding to take place, the term ‘voiding dysfunction’ becomes inclusive and will be used by this author throughout this discussion.

### **Voiding function and dysfunction: Anatomy, histology, physiology, and pharmacology**

Both the normal and pathologic anatomy and the histology of the lower urinary tract have been well delineated.

The function of the lower urinary tract is to allow efficient collection, storage, and voluntary, complete voiding of urine. During normal bladder filling there is a minimal rise in intravesical pressure despite the ongoing increase in volume; at the same time, a gradual increase in urethral resistance occurs. In the normal circumstance, there is no involuntary contractile detrusor activity and increases in intra-abdominal pressure do not cause urinary leakage. Prior to reaching bladder capacity, the sensation of bladder filling is perceived by the child and urination is voluntarily initiated; micturition proceeds to completion, with a decrease in bladder outlet resistance and contraction of the bladder smooth musculature.



Wein has observed<sup>1</sup> that the pathophysiology produced by an abnormal clinical state can often be explained according to a part of one theory of voiding but one should not take this to mean that the entirety of the theory is correct. After reviewing the literature, which contains many conflicting models of urinary tract function, the reader will have to adopt those precepts that are clinically and/or scientifically most useful to the situation at hand.

### **Anatomy of the bladder**

Both Galen and daVinci were interested in how human beings 'collected' urine and how the bladder emptied itself. Early on, the observation was made that the bladder contained three layers: an outer connective tissue layer, a set of smooth muscle layers, and mucosa lining the interior of the bladder. Classically, the smooth muscle of the bladder is considered to have two components: the detrusor and the trigone. The trigone is that region of the posterior bladder wall generally considered to be between the ureteral orifices and the bladder neck; it is further divided into the superficial area and deep trigone. Most observers believe that the detrusor is organized at the bladder base as an outer longitudinal, a middle circumferential, and an inner longitudinal layer. The superficial layer of the trigone is usually considered to be ureteral in origin, whereas the remainder of the outer musculature is endodermal. The anatomy of the ureteral orifice is considered elsewhere in this book.

### **Anatomy of the urethra**

The male and female urethras differ from each other considerably and will be described separately. The pediatric female urethra varies in length from about 8 mm in a term female to upwards of 4 cm in length and 6 mm in diameter in a postpubertal adolescent girl. It is embedded in the anterior aspect of the vagina, and consists of an outer muscular layer and an epithelium. The urethral epithelium at rest consists of longitudinal folds that are apposed to each other during the storage phase of the bladder. There is an inner longitudinal smooth muscle portion which extends throughout the length of the female child's urethra and there may or may not be an outer circular or semicircular layer; this is debated among anatomists. The smooth muscle of the pediatric female urethra is embedded in a matrix of collagen that is considered by most to be the major structural component.

The male urethra in a child is classically divided into anatomic segments. The preprostatic urethra is only a few millimeters in length in the newborn male child but grows to 1.5 cm in length in adolescence. It contains smooth muscle bundles generally oriented in a circular arrangement that becomes continuous distally with the prostatic capsule; these muscle bundles are separated by connective tissue. The prostatic urethra is between 6 and 8 mm in length in a newborn male, growing to 2 cm in length in an adolescent. The membranous urethra is only 1 mm or so in length in the newborn male and may extend distally into the bulb of the penis. Some anatomists perceive longitudinal and/or circular fibers in the membranous urethra, while other observers are not in agreement. The anterior urethra is distal to the membranous portion and functions purely

as a conduit; it is generally considered not to have a role in either maintaining continence or facilitating bladder emptying.

There is continuity between the bladder and urethra. The extension of the supravescical trigone layer into the urethral wall has been well described, and suggests that the opening of the bladder neck and proximal urethra during active bladder contraction is based in part on passive anatomic factors. The external sphincter has a voluntary striated muscle component that allows interruption of urinary flow in normal children.

In the male, the sphincter is described as completely annular, although decreased in its posterior component, as it blends with the fibers of the prostatic capsule, while in the female the area is described as tapering considerably and being deficient posteriorly. The intrinsic segment is often referred to as the rhabdosphincter and readers are referred to more in-depth discussions of the functional anatomy.<sup>2</sup> In both boys and girls, the caudal end of the striated component is adjacent to a bulky skeletal muscle structure oriented in the horizontal plane in the pelvic floor encircling the membranous urethra. This corresponds to what is described in standard anatomy textbooks as the external urethral sphincter. The presence of an intrinsic striated component is also agreed upon by most observers. The striated sphincter is generally considered to comprise both the intramural and intrinsic striated components of the female child's urethra and the posterior urethra in the male child.

Despite older observations in the literature, it is now generally regarded that the bladder neck does not contain an anatomic sphincter. Pseudosphincteric action at the bladder neck is thought to be due to the inherent tension exerted by elastic fibers in this area on the lumen of the bladder neck.

An understanding of the physiology and cellular biology of smooth and striated muscle relevant to the lower urinary tract is important in understanding the normal function of this region. Not only are structural innervation and neural control of muscle function important but also one must be aware of more basic concepts such as tonus, excitation-contraction coupling, and viscoelasticity. Knowledge of neurotransmission and receptors is also crucial. These issues are beyond the scope of this chapter.

### **Anatomy of the gross peripheral innervation of the lower urinary tract**

The bladder and urethra are supplied by efferent parasympathetic and sympathetic neurons through the pelvic and hypogastric nerves. Both of these bear afferent (sensory) neurons from the bladder and urethra back to the spinal cord. The pelvic nerve usually has three or four trunks that branch on either side of the rectum. Efferent sympathetic nerves traverse lumbar sympathetic ganglia and join the presacral nerve. This complex then divides into the left and right hypogastric nerves. The inferior hypogastric plexus is formed by a meeting of the hypogastric and pelvic nerves. Various branches of this plexus innervate the pelvic organs. Afferent neurons are borne by both the hypogastric and pelvic nerves to the lumbosacral spinal cord and by dorsal columns, reaching the spinal cord through either dorsal or ventral roots.

Efferent innervation of the striated sphincter is derived from the sacral spinal cord by means of the pudendal nerve. Whether the pudendal nucleus is the only motor center or not is debatable. The autonomic nervous system may also help innervate these muscles.

Neural and humoral influences on lower urinary tract function, including receptor distribution, stimulation, and blockade, are being elucidated through the use of animal models, and are beyond the scope of this discussion.<sup>3</sup>

### *Central nervous system control of the lower urinary tract*

Voiding is a function of the peripheral autonomic nervous system. Final definitive control of lower urinary tract function however resides at higher neurologic levels. The spinal cord, brainstem, cerebellum, and basal ganglia may all exert functional control of the lower urinary tract. Likewise, very sophisticated laboratory experimentation has shown that there is a role for the thalamus, hypothalamus, limbic system, and cerebral cortex. Organization of the micturition reflex, including the possible role of the supraspinal micturition center and sacral areas, are key to the understanding of both normal and abnormal voiding. There are at least six component reflexes of micturition.<sup>4</sup>

### **Clinical considerations**

Wein et al have delineated several functional questions regarding urinary tract function.<sup>5</sup> The following questions and answers are based on these queries.

**What determines bladder response during filling?** The normal bladder responding to filling at a physiologic rate produces minimal change in intravesical pressure until capacity is approached. Normally, excellent compliance is brought about during the early stages of bladder filling by quiescent characteristics of the bladder wall. When the filling volume exceeds the rate of stress relaxation, the viscoelastic properties of the bladder wall allow for an increase in intravesical pressure. Therefore, there is little or no rise in bladder pressure until bladder capacity is approached. These phenomena can be explained by the classically demonstrated inherent responses of smooth muscle to stretch.

Partial bladder outlet obstruction can bring about a reduction in bladder capacity and compliance. This is thought to be due to intramural infiltration of connective tissue. We have previously documented that this can result in poor compliance that is unresponsive to pharmacologic manipulation, and this group may require bladder augmentation.<sup>6</sup>

The interplay of inhibitory neural mechanisms and prostaglandin release contributes significantly to both the filling and storage phase of micturition. Wein and Hanno have pointed out the existence in animals of a spinal sympathetic reflex, which is evoked by bladder filling.<sup>7</sup>

**What determines outlet response during filling?** Landmark experimentation, occurring through the 1960s into the 1980s, brought about agreement that there is a gradual rise in urethral/bladder neck pressure during bladder filling. Unfortunately, both in an experimental and clinical setting, the measurements of urethral pressure and concomitant definitions are difficult and nonstandardized. Separation of the smooth and striated muscular contributions to urethral pressure is unreliable. Various authors have tried to arrive at estimates of urethral pressure components by looking not only at striated and smooth muscle but also at vasculature and connective tissue; these derivations have not produced a consensus.

There is a demonstrable interaction of the passive properties of the urethral wall with a continuity of smooth muscle from the bladder base. Most observers believe that bladder

filling increases bladder neck tension and that this is then conveyed to the urethra and mirrored by tonal changes in the urethral wall. Prostaglandins released from the bladder mucosa and bladder musculature during filling may also raise urethral resistance.

**Why does urinary leakage not occur with increases in intra-abdominal pressure?** It has been well demonstrated that during voluntary micturition, bladder pressure becomes higher than outlet pressure; thereby, accommodative changes occur in the configuration of the bladder outlet, and urine passes into and through the proximal urethra. It has been pointed out that coordinated bladder contraction does not occur in response to changes such as intra-abdominal pressure brought about by Valsalva maneuver. Urine flows into the proximal urethra by coordinated bladder neck relaxation along with an increase in intravesical pressure. This comes about through a neurally mediated reflex mechanism that is associated with resistance changes in the bladder neck and proximal urethra. It has been further demonstrated that any increase in intra-abdominal pressure is uniformly transmitted to the proximal urethra. It has also been shown that increases in urethral closure pressure noted with incremental extrinsic pressure applied to the abdomen are greater than the extrinsic pressure employed. This indicates that there is active muscular function in addition to simple passive pressure transmission involved. Both the smooth muscle and striated sphincter are thought to be involved.

If one considers the bladder neck and proximal urethra as a sphincter unit, the anatomic location of the structure helps explain positive transmission. At least in the female, the sphincter unit is thought to be abdominal as opposed to pelvic in location and thereby permits pressure transmission. There are, however, those who have questioned the validity of these explanations.

**Why does voiding ensue with a normal bladder contraction?** It has been confirmed that there is reflex correlation between a voluntarily induced bladder contraction of adequate magnitude and the active response of the proximal urethra. Electromyography (EMG) has clearly demonstrated a decrease in pelvic floor striated muscle tonus before voluntary bladder contraction initiation, which suggests that this decrease is brought about by a reflex mechanism involving the striated sphincter and mediated through the pudendal nerve. It is also most often thought that a similar coordination of smooth muscle sphincter activity comes about, presenting itself as a decrease in efferent hypogastric nerve activity. Whether this mechanism is brought about by excitation of adrenergic receptors or not is debatable.

### *Diagnosis and classification of voiding dysfunction*

One of the most difficult aspects of the treatment of voiding dysfunction in children is determining whether one is dealing with what will be a self-limiting problem or whether the voiding dysfunction is a symptom complex of a more severe underlying problem. A thorough history is required, stressing whether the problem occurs day and/or night; whether there is urgency, frequency, hesitancy, 'pressure', or dysuria; whether the child wets the bed at night or self-arouses and then voids (true nocturia); whether a family member has observed the child's urinary stream; and whether the child is ever noted to strain to void (stranguria). It is important to know whether the child has ever had a documented urinary tract infection (UTI) or not. Time of onset of the symptoms (primary

or secondary) is important. Also, one must ask if the symptoms have changed over time and if so, how?

A complete physical examination is necessary, with a 'quick' genitourinary neurologic examination (Table 61.1). Special attention should be paid to the back and sacrum. Often in severe, recalcitrant cases, the author will suggest consultation with a pediatric neurologist. Both a dipstick and a microscopic urinalysis are performed. Urine culture and sensitivity is only undertaken in the case of an abnormal urinalysis or a history of UTI. A simple ultrasonic residual urine should be obtained on the initial visit.

In cases of nocturnal enuresis only, the evaluation may stop here and treatment ensue. In more complicated cases, modest imaging may be ordered, such as a renal and pelvic ultrasound; special attention should be paid to the thickness of the bladder wall on pelvic ultrasound. A voiding cystourethrogram (VCUG) is ordered if the child has had a UTI. Suspected back/spinal abnormalities are evaluated by bony films and magnetic resonance imaging (MRI) if needed. Endoscopic evaluation is limited to refractory cases or if an obstructive component is suspected. The author employs a fairly high index of suspicion for obstructive causes of micturitional abnormalities, having seen a plethora of these overlooked by previous treating urologists. There seems to be an unwarranted avoidance of simple cystoscopy in this group, bringing about delayed diagnosis and treatment.

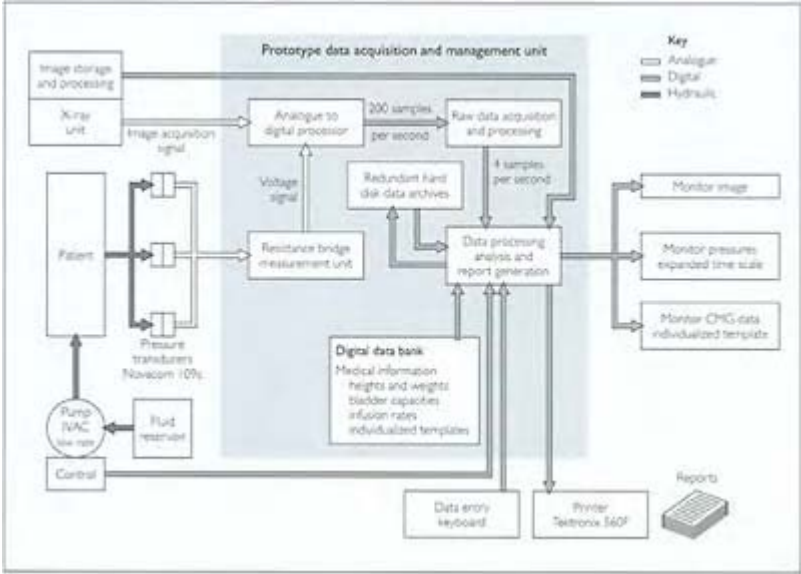
Urodynamics are used only if initial empiric therapy fails or the case is severe. Attention is drawn to the algorithm of Wahl et al (Figure 61.1). Repeat urodynamics after several weeks/months of treatment are often helpful but the child's symptomatic response is a better gauge of therapy success.

Special urodynamic tests such as those relying on super-sensitivity to parasympathomimetic agents, or anticholinergic stimulation may be helpful but this author has found them hard to interpret and cumbersome. Electromyography and evoked potentials may be helpful and this author leaves those studies to the neurologist; these investigations are less popular now than previously as they have been found to be of minimal therapeutic benefit. Simple flow rate determination, on the other hand, may be very useful and it is the recommendation of this author that all pediatric urologists have that capability readily available.

Historically, numerous attempts have been made to classify voiding dysfunction. All classification systems have their champions and detractors, but they all suffer from

**Table 61.1** *'Quick' genitourinary neurologic examination*

| Test                                 | Normal response      | Abnormal response                 |
|--------------------------------------|----------------------|-----------------------------------|
| Back examination                     | Grossly normal spine | Dimple(s), hair tufts, hemangioma |
| Lower extremity deep tendon reflexes | Normal               | Absent or clonic                  |
| Bulboeavermosis/clitroanal reflex    | Present              | Absent or hyperactive             |
| Genital pinprick                     | Normal               | Absent                            |
| Perigenital light touch              | Normal               | Absent or paresthetic             |
| Hot/cold water                       | Normal               | Absent or paresthetic             |
| Anal tone                            | Present              | Lax or clonic                     |
| Observation of ambulation            | Normal gait          | Various forms of abnormal gait    |



**Figure 61.1**  
Wahl's urodynamic methodology.  
(Reproduced with permission of  
Wahl.)

some deficiency. This author prefers the functional system shown in Table 61.2. As one initially evaluates a child, then looks for landmarks of success or failure of the treatment regimens, reliance on this classification is most clinically relevant.

**Table 61.2** *Functional classification of voiding dysfunction*

- Failure to store:
    - Because of the bladder
    - Because of the outlet
  - Failure to empty:
    - Because of the bladder
    - Because of the outlet
- Source: Modified from Wein et al.<sup>5</sup>

*Treatment of voiding dysfunction*

The old adage that ‘children are not small adults’ is applicable here: not only are the problems different but also one is dealing with the role of organ maturation and changing physiology as the child grows. Goals of management should always be clearly understood by the care team and the family (Table 61.3). The author will give a brief

overview of current pharmacologic intervention options, review some behavior modification techniques, but will not, for instance, re-examine all the surgical options available, only the more recent minimally invasive ones. Anticholinergics have long been our mainstay when using the pharmacologic option for control of voiding dysfunction. Oral oxybutynin has led the way since its introduction; its extended-release formulation is helpful in older children. Anticholinergic agents developed earlier serve as second-line therapy. More recently introduced, tolterodine can be very effective, but does not come as a

**Table 61.3** *Goals of treatment in voiding dysfunction*

|   |
|---|
| Normal bladder control                  |
| No catheter or stoma                    |
| Preservation of renal function          |
| Absence of urinary tract infection      |
| Adequate urine storage at low pressure  |
| Complete urine emptying at low pressure |
| Educational/vocational adaptability     |
| Social/peer group satisfaction          |

liquid, so is limited as to age usage. When compared to oxybutynin, the author has found fewer side-effects with tolterodine in age/symptom-matched patients, especially dry mouth.

In children with neurologically or functionally increased outlet resistance,  $\alpha$ -adrenergic blocking agents may play a role.

When incomplete bladder emptying is part of the clinical picture, oral bethanechol continues to be the pharmacologic mainstay, but again is limited in the pediatric population because of a lack of a liquid form. Intermittent catheterization continues to be useful in select patients.

Increased outlet resistance is needed in some children with poor bladder neck/urethral tone and this can often be accomplished with either physiotherapy (modified Kegel's exercises) or pharmacologically with agents such as pseudoephedrine. Success rates with both these approaches can be excellent, although one has to watch the patient's blood pressure closely when using pseudoephedrine.

Collagen-derivative injection therapy to the bladder neck and proximal urethra to 'bulk up' the outlet has met with, at best, only modest success. Open procedures such as vesicourethral suspension, 'slings', and use of the artificial sphincter have limited but definitive roles in managing these children and treating physicians should be well versed in these techniques.

**Innovations in minimally invasive management of voiding dysfunction**

**Diagnostics.** No matter what new treatment modalities may arise, the applicability of such treatments only attains a level of success if based on the soundest, most-reliable information obtained from diagnostic tools. Urodynamics must be improved, especially

in ways that are minimally invasive; per urethram urodynamics are self evidently nonphysiologic due to the presence of a foreign body in the bladder. Noninvasive, suprapubic ultrasonic sensing equipment is being developed and, if made reliable, will add considerably to the diagnostic armamentarium. The role of uroflowmetry will continue to be paramount; more dependable, cost-effective flowmetric instrumentation is being developed.

**Newer pharmacologic agents.** For the foreseeable future, anticholinergics will continue to be the pharmaceutical of choice when detrusor relaxation is needed. The extended-release forms now available are of considerable help. Two new forms of oxybutynin are in development: a topical transdermal delivery patch and S-oxybutynin, which is formulated to improve tolerability when compared to the currently available form.

Further work is also being done with other pharmacologic agents for improved formulations and alternative delivery systems, production of selective receptor antagonists, neuronal desensitizing agents, CNS receptor remodelers, and channel-active agents. Several pharmaceutical houses are also trying to develop dual-acting or combination therapies. Time-release intravesical anticholinergics may soon be inserted once a month, the way urethral suppositories were in the past.

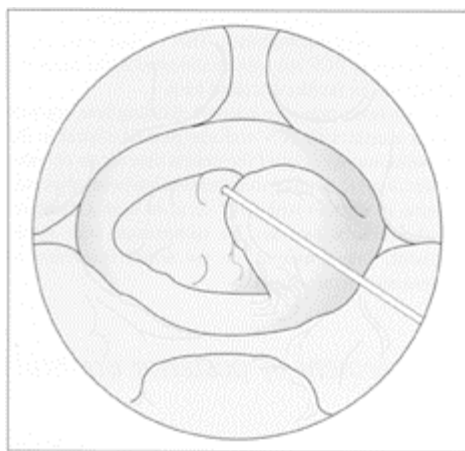
**Endoscopic/injection therapy advancements.** As has already been mentioned, manufacturers of cystoscopes and laparoscopic equipment are diligently striving to develop small-caliber instrumentation with finer optics, although 2 mm is the smallest attainable so far. Even those instruments are difficult to use because of their malleability and fragility.

Like most observers, this author has been displeased with injection therapy for incontinence using collagen derivatives. Other intrinsically natural agents such as autologous fat, myoblasts, and chondrocytes have been used with minimal success. Polytetrafluoroethylene (Teflon) has been used with moderate success, although it has received bad press because of particle migration. Our European colleagues have achieved very good results with endoscopic injection of polydimethyl siloxane (Macropastique) and authorization for use of this agent in the United States is being sought.

The approval of newer bulking agents such as pyrolytic carbon-coated zirconium beads (Durasphere) and dextranomer/hyaluronic acid microspheres (Deflux) seems to offer promise, although usage and long-term evaluation in children is still on the horizon. Other compounds tried with limited success have been ethylene vinyl alcohol, bioglass, and silicone microballoons.

**Laparoscopic bladder procedures.** Two procedures have gained some favor. Our group has been very pleased with the long-term results of laparoscopic bladder autoaugmentation (LBAA) (Figure 61.2). We have performed 17 LBAA's with good-to-excellent results in all but 2 children. Patient selection and preventing postoperative urinary extravasation are the two predictors of successful outcome.<sup>8</sup>





**Figure 61.2**

Laparoscopic bladder autoaugmentation. The bladder is seen through an umbilical camera port looking down into the pelvis. The top is anterior, the bottom (rectum in view) is posterior. The laparoscopic grasper is holding the detrusor elliptical flap, which has been partially dissected off the mucosa; the mucosa can be seen bulging to the left of the flap.

Laparoscopic bladder neck suspension (modified Burch) has been used in a few older girls with true stress incontinence and in a few spina bifida females. After some early enthusiasm, indications have been more limited, as, in most hands, the laparoscopic approach offers much less long-term success than open procedures.

**Biofeedback and neuromodulation.** Behavioral modification has taken a step forward with the development of game-playing software for children. The group which advanced the software has reported excellent results with its use.

Neuromodulation embraces a wide variety of treatment modalities. Down-regulation of the sacral reflex arc which influences voiding is the goal of all these forms of therapy. Bower et al<sup>9</sup> recently reported their experience with adjunctive neuromodulation in children. Further developments in this area are to be expected.

**Robotic surgery/computer assisted surgery.** The future of robotic surgery and computer-assisted surgery holds unlimited opportunities. It is not too far removed from robotic biopsy—which has already been done—to robotic resection.

Microelectrical mechanical systems (MEMS) also offer advances in pediatric urologic surgery. Most of these devices are less than the size of a human hair. The future of these

modalities as both sensors and actuators is limitless. Stereotactic radiosurgery combined with telemedicine may allow totally off-site surgery in the future.

### **Posterior urethral valves**

If one defines posterior urethral valves (PUV) as any congenital narrowing of the distal prostatic urethra, a considerable spectrum of abnormalities presents itself. Historically, Young et al<sup>10</sup> classified three types of PUV, only one of which is now universally recognized to exist. The diagnosis and treatment of PUV has always been a significant challenge. Accepted endpoints of management are not agreed upon other than generally endorsing the view that normal micturitional control and preservation of renal function are conclusive goals.

Treatment of PUV with minimally invasive techniques was an accepted challenge from the onset of diagnosis of the entity. Early treatment often involved performing a cytotomy and fulgurating the valves from above.

The incidence of valves seems to correlate closely with one's predilection for diagnosing them: the more open one is to the possibility that any narrowing in the posterior urethra may be valves, the higher one accepts the incidence thereof. The best postulation the author can arrive at from various sources is that valves have an incidence range of 1 in 5000–8000 boys.

### *Embryology*

PUV have no known genetic basis and are rarely familial; however, there are a few reports of twins with valves and the author has seen 3 male siblings with PUV. Even in identical twins, only one may be affected. Uncommonly, other organ system anomalies may be reported.

To understand the embryology of PUV, one must be grounded in the formation of the normal genitourinary tract. Many theories as to how PUV evolve have been proposed. One of the earliest, and still a theory with many adherents, is that PUV are a persistence of normal urethral folds. This serves as at least a partial explanation of Young's type I valves but does not explain, among other presentations, diaphragmatic valves.

It is also believed by some that valves are remnants of the urogenital membrane or that valves are a result of an abnormal melding of the ejaculatory duct, which is wolffian in origin, and the prostatic utricle (müllerian in origin). Causation by an abnormal insertion and persistence of the distal aspect of the wolffian system has also been postulated.

### *Diagnosis and classification*

Diagnosis of PUV is now often made in utero and, on occasion, also treated before birth.

There are overabundant presenting signs and symptoms in any group of boys found to have valves. Urinary symptoms can be as meager as 'urinary dribbling' and as striking as urinary extravasation and ascites. UTIs are a common presentation. Uncommonly, neonatal hematuria and azotemia may be seen in babies later found to have valves. Nonurinary manifestations such as vomiting (and other gastrointestinal symptoms),

respiratory distress, edema, failure to thrive, and seizure disorders may be seen. Older boys tend to present with a wider array of symptoms and often the symptoms may be less definitively urologic, such as malaise and growth retardation. Enuresis and vague voiding dysfunction are also often seen at presentation in older boys.

Abnormal physical findings may vary from palpable kidneys and an ascitic abdomen to a palpable bladder. A distended abdomen may be seen, and perhaps noted not uncommonly are signs suggesting renal insufficiency. On occasion, no abnormal physical findings are described.

Laboratory studies are usually not helpful at time of diagnosis but are needed as baselines to follow the child with valves. A serum creatinine, a set of electrolytes, and a complete blood count (CBC; especially looking for anemia) are all initially necessary. The urine should be serially evaluated for protein, blood, and the presence of infection.

The VCUG is the study of choice for diagnosing PUV. Several other abnormalities need to be considered in the differential diagnosis of PUV. Various discoordinate types of voiding dysfunction, especially external sphincter dyssynergia, may produce cystographic patterns similar to PUV. Conditions such as variants of mixed incomplete abdominal musculature (prune-belly syndrome) may also radiographically appear similar to PUV. Polyps of the verumontanum are uncommon, but not rare. Also, on occasion, VCUG patterns seen in boys with neurogenic bladder and meatal stenosis may mimic PUV. Boys with severe non-neurogenic voiding dysfunction (the Hinman syndrome) may in certain circumstances have VCUGs easily confused with PUV.

To further perplex the issue, there are boys with mild PUV who may have a misrepresentative appearance of the urethra on VCUG. These are often older children with enuresis. At cystoscopy, the valves may be visually quite pronounced and not correlative with the VCUG. There are many anecdotal reports of this phenomenon.

Cystoscopy plays a paramount role in the diagnosis and treatment of PUV. One should have a high index of suspicion for the existence of valves in boys who have not responded to empirical treatment for such entities as voiding dysfunction. One should also be prepared to endoscopically treat valves at the time of cystoscopy to avoid a second anesthesia/sedation. The variant endoscopic appearances of PUV are well documented in the literature and will not be further discussed here.

Urodynamics may play a role in deciding how urgently to treat a child with PUV and also may be critical in the long-term management of the sundry aberrances of 'valve bladder'. A set of baseline urodynamics has been advocated by some in all boys with PUV so as to have a predetermined reference data set for comparison with future treatment. One is referred to the earlier discussion of urodynamics in this chapter.

### *Management of posterior urethral valves*

Complete obliteration of obstructive valve tissue is the goal of all types of treatment. Prior to the invention of the infant resectoscope, open techniques for excision with surgical exposure of the posterior urethra were carried out. This often involved symphysiotomy. Due to bleeding, poor visualization in the surgical field was often encountered, the valves inadequately visualized, and frequently open resection was insufficient, leaving behind obstructive valve remnants. Postoperatively, it was not infrequently noted that the sphincter had been damaged.

Now, endoscopic resection or incision of the valves is usually a straightforward procedure in the hands of adequately trained pediatric urologists. Often it is the only treatment necessary to abolish the valves and problems concomitant to them.

Refinement of the techniques and miniaturization of instrumentation for endoscopic management of PUV have allowed the treating surgeon to successfully carry out valve ablation in most boys, save the very smallest premature male infants. This has been one of the most rewarding developments in minimally invasive surgery in pediatric urology. These advancements will be dealt with below. While such preparations are being undertaken, or as a part of the initial treatment, bladder drainage may be necessary. Historically, this has been accomplished by temporary per urethram placement of an appropriate-size polyethylene feeding tube. Lately, as manufacturing techniques have been perfected, Foley catheters as small as 6 F have been universally available (in some locales, 4 F Foley catheters are being used). Foley catheterization may be preferred for a closed system in all but the most premature infant. Cutaneous vesicostomy may be necessary in some children, although the indications for such have greatly narrowed over the last few years.

Children with PUV who have concomitant hydroureteronephrosis have always presented formidable and controversial management problems. Mild-to-moderate hydroureteronephrosis often resolves after valve ablation. But in children with severely dilated, possibly aperistaltic ureters, management is much more challenging. After valve ablation, some of these children will resolve their ureteral dilation, but unremitting severe hydroureteronephrosis may in the long run contribute to renal insufficiency in some PUV children and require interventional drainage. Dialysis and renal transplantation continue to be required in a subset of boys with PUV no matter how well they are managed early on.

It is the author's advice that when a decision has been made for upper tract diversion, percutaneous approaches are preferred over open techniques such as loop ureterostomies or pyelostomies.<sup>11</sup> Often percutaneous techniques can be employed without requiring a full general anesthesia, using only local procaine-derivative injection with anesthesia standby with sedation. All forms of upper urinary tract diversion, however, must be looked upon with a jaundiced eye, as many institutions have reported that such diversion did not improve the child's long-term outlook.

### *Minimally invasive valve ablation techniques*

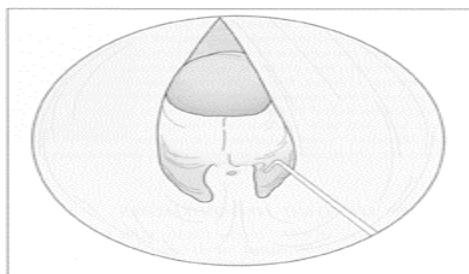
Historically, ablation of PUV was quite cumbersome and resulted not infrequently in damage to the urethra with an iatrogenically induced lifelong problem with urethral stricture disease, among the likelihood of other problems. One malady—PUV—was traded for another—a urethral stricture. Often, instruments used were the smallest adult resectoscopes, originally designed for resection of adult benign prostatic hyperplasia or bladder tumors.

As the instruments were too large in caliber to be inserted per urethram, a perineal urethrostomy was advocated by some. Open resection from a retropubic approach was promoted by others. Use of an otoscope and 'blind' valve destruction with sounds, metal stylets, or hook electrodes—some employing diathermy—also had their adherents. Rupture with balloon catheters was advocated. On occasion, crude (by today's standards)

radiographic techniques were used to assist, converting these techniques to 'semi-blind'. Even wishful thinking was employed in hopes that an indwelling Foley catheter 'for some weeks' would lead to destruction of the valvular folds by ulceration.<sup>12</sup>

This author's technique involves taking the child to the cystoscopic suite and having the pediatric anesthesiologist administer a light general anesthetic, usually by face mask or LMA (laryngeal mask airway) unless the child has renal insufficiency/electrolyte problems—then an endotracheal tube may be used. If the child is not in hospital, the procedure is done as an outpatient/same-day surgery. In babies, the 9 F infant resectoscope is introduced into the bladder; a larger scope is used for older boys. A meatotomy may be necessary. The obturator is left in the sheath, which is heavily lubricated prior to passage. The obturator is removed, the bladder drained, and the working element with 30° Hopkins optics inserted. Either a video camera or direct telescopic examination may be carried out; the author recommends one use whichever method gives the resectionist the best vision. The bladder is closely inspected for trabeculations, ureteral orifice configuration, or other abnormalities and the scope is then pulled gently down the urethra until the valves are visualized. The bladder neck and prostatic urethra are evaluated en passant, paying close attention to any contracture or hypertrophy of the former and the degree of dilation in the latter. Optics are then changed to the 0° lens to allow the resectionist at least two different views of the valvular structure.

One valve at a time is then engaged with the right-angle electrode at either the 5 o'clock position (left valve), or the 7 o'clock position (right valve) (Figure 61.3). While the author prefers the right-angle electrode, a loop, bugbee, or other type electrode may produce equal results in the hands of others. Endoscopic solution should be flowing antegrade through the open scope port to balloon-out the valve. Close attention is paid to the location of the external urinary sphincter and assurance attained that it is not violated during the procedure.



**Figure 61.3**

View of the posterior urethra with valve leaflets on either side. The tip of the pediatric resectoscope is just inside the sphincter. The elevated, hypertrophic bladder neck may be seen distally, the verumontanum

proximally, and the moderately dilated prostatic urethra between. The right-angle electrode is preparing to engage the left valve leaflet (to the viewer's right).

The valve is then 'pop-buzz' incised. Pop-buzz involves using fairly high cutting current and very rapidly tapping of the power source foot pedal while the valve is engaged under minimal pressure. This usually destroys the valve, much as cutting a billow of a parachute. The floor of the urethra where the incision occurred is then closely inspected to be sure the entire valve leaflet has been destroyed. Additional pop-buzz swipes may be necessary. Care is taken to be sure the swipes are not too deep. When each of the valves is destroyed in this fashion, the 12 o'clock position of the urethra is closely scrutinized and if any obstructive tissue is noted, it is dealt with in the same manner. Any bleeding is strictly controlled by turning off the solution flow and inspecting the base of the incision area, gently coagulating it with low current as necessary. A Foley catheter is rarely left in, only if the resection has been difficult, or bleeding control challenging. The child is discharged home as soon as he voids.

The author has used this technique for resection of PUV in 105 boys, 11 of which were secondary resections following continued obstruction after primary resection by other urologists. A catheter has been left only six times (94.3% catheter-free resections). On one occasion, a child bled 20 hours post-resection, was catheterized, and did well with the catheter removed 2 days later. Long-term outcome has been excellent, as per voiding and renal function criteria. Only 3 boys have required repeat ablation (2.9%).

In follow-up, close attention is paid to voiding habits, flow rate, and residual urine (measured by ultrasound). A post-resection cystogram is not necessary if the ablation was straightforward, the child is asymptomatic with normal micturitional control, the upper tracts and serum chemical parameters were normal, and there were no/nil bladder trabeculations noted at cystoscopy prior to ablation. If these criteria are not met, follow-up cystography may be indicated. 'Routine' post-ablation cystograms only serve to reassure the physician and are most often unnecessary.

#### *Future unique innovations*

Better treatment of PUV in the future with less operative complications is contingent upon the ability to further miniaturize the instrumentation employed. It may be that up to two-thirds of PUV are now diagnosed prenatally. In future, that may rise to >90%. Better maternal/fetal diagnostic ultrasonography is to be expected. The challenge however is to determine whether earlier management will ameliorate long-term outcome.

Other prognostic modalities will need to improve to aid in better management of PUV. Advances in noninvasive sonographic diagnosis will continue to be made.<sup>13</sup> Likewise, progress in applications of MRI to urethral abnormalities will proceed.<sup>14</sup> The evolution of miniaturization of pediatric urologic instruments has been one of our greatest technological advances. This progress continues. There is now a 4.5 F blunt needle cystoscope commercially available. Companies in the endoscopic market continue to

work to develop resectoscopes smaller than 9 F and prototypes are obtainable. Instrumentation as small as 2 mm has been successfully used in laparoscopy and one would hope such could be eventually applied to transurethral devices. A cut-down version of a 6.9 F semi-rigid ureteroscope has been adapted for use in treating PUV (pers comm).

Several commercial experimental analyses of newer power sources for application to valve ablation are being considered. The Harmonic Scalpel (Ethicon Endo-Surgery, Inc., Cincinnati, Ohio), already with many accepted applications in laparoscopy, is undergoing testing for transurethral adaptation. Pulsed radiofrequency waves may also offer PUV treatment prospects. Various laser sources are always under consideration with the major difficulty encountered in transurethral use in children being the limiting of depth penetration of the laser and resultant periurethral damage.

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## 62

# Intersex

Thomas F Kolon

### Diagnosis

An individual's chromosomal sex is established at fertilization; chromosomal sex then directs the undifferentiated gonads to develop into either testes or ovaries. A patient's phenotypic sex results from the differentiation of internal ducts and external genitalia under the influence of hormones and transcription factors. If there is any discordance among these processes (i.e. chromosomal, gonadal, or phenotypic sex determination), then ambiguous genitalia or intersexuality develop. Currently, there are four main categories of intersex that are described: female pseudohermaphroditism (FPH); male pseudohermaphroditism (MPH); gonadal dysgenesis, either pure (PGD) or mixed (MGD); and true hermaphroditism (TH).<sup>1-3</sup>

#### *Female pseudohermaphroditism*

Female pseudohermaphroditism is the most common intersex disorder. The patient's ovaries and müllerian derivatives are normal and the sexual ambiguity that is seen is limited to masculinization of the external genitalia. A female fetus is masculinized only if she is exposed to androgens and that degree of masculinization is determined by the stage of sexual differentiation at the time of exposure (Figure 62.1). Masculinization may also uncommonly be secondary to exogenous maternal steroids.

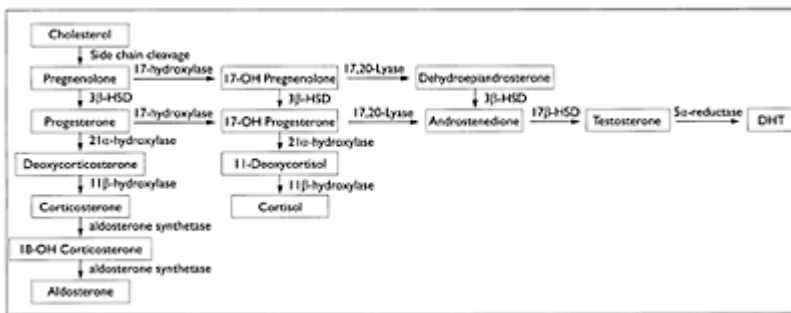
Congenital adrenal hyperplasia (CAH) accounts for the majority of FPH patients. Inactivating or loss of function mutations in five genes involved in steroid biosynthesis can cause CAH: CYP21, CYP11B1, CYP17, HSD3B2, and StAR (Figure 62.2). While all six of these biochemical defects are characterized by impaired cortisol secretion, only CYP21 and CYP11B1 are predominantly masculinizing disorders, with HSD3B2 to a lesser extent. Although the female fetus is masculinized due to overproduction of adrenal androgens and precursors, the affected males have no genital abnormalities. In contrast, HSD3B2, CYP17, and StAR deficiencies block cortisol synthesis and gonadal steroid production. Thus, affected males have varying degrees of MPH while females generally have normal external genitalia. Each of





**Figure 62.1**

46XX patients with mild (A) and moderate (B) masculinization due to congenital adrenal hyperplasia.



**Figure 62.2**

The intersex steroid biosynthetic pathways with responsible enzymes. 3 $\beta$ -HSD=3 $\beta$ -hydroxysteroid dehydrogenase; 17 $\beta$ -HSD=17 $\beta$ -hydroxysteroid dehydrogenase; DHT=dihydrotestosterone.

these genetic defects are inherited in an autosomal recessive pattern.<sup>4-6</sup>

Deficiency of CYP21 is the most common cause of genital ambiguity. Two CYP21 genes are located on chromosome 6 between HLA-B and HLA-DR: a functional CYP21B gene and a CYP21A pseudogene that is nonfunctional due to its encoding of multiple stop codons. Recombination between CYP21B and the homologous but inactive CYP21A accounts for approximately 95% of 21 $\alpha$ -hydroxylase deficiency mutations.<sup>7</sup> A transfer of CYP21A sequences to CYP21B is present in 80% of patients resulting in a

variable decrease in 21 $\alpha$ -hydroxylase activity. These conversions usually involve the transfer of inherent CYP21A mutations. Patients with simple masculinizing 21 $\alpha$ -hydroxylase deficiency have been identified with a conversion mutation causing severely decreased enzyme activity but sufficient aldosterone production to prevent salt wasting.<sup>8-10</sup>

CYP11B1 encodes 11 $\beta$ -hydroxylase, which converts 11-deoxycorticosterone to corticosterone and 11-deoxycortisol to cortisol.<sup>9</sup> Alternatively, CYP11B2 encodes for aldosterone synthetase, which converts deoxycorticosterone (DOC) to corticosterone and 18-hydroxycorticosterone to aldosterone. It is expressed in the zona glomerulosa and is under the influence of angiotensin II and potassium. Cortisol deficiency results in increased secretion of 11-deoxycortisol, DOC, corticosterone, and androgen by the adrenal gland. Hypertension, which occurs in about two-thirds of patients, is presumptively a consequence of excess DOC, with resultant salt and water retention. Excess androgen secretion in utero masculinizes the external genitalia of the female fetus. After birth, untreated males and females progressively virilize and experience rapid somatic growth and skeletal maturation.

3 $\beta$ -hydroxysteroid dehydrogenase (3 $\beta$ -HSD) catalyzes pregnenolone to progesterone and dehydroepiandrosterone (DHEA) into androstenedione.<sup>6</sup> Complete deficiency of 3 $\beta$ -HSD impairs synthesis of adrenal aldosterone and cortisol and gonadal testosterone and estradiol. These newborns have severe CAH and exhibit signs of mineralocorticoid and glucocorticoid deficiency in the first week of life. Affected females have mild-to-moderate clitorimegaly and males exhibit ambiguous genitalia with variable degrees of MPH (hypospadias, cryptorchidism, penoscrotal transposition, blind vaginal pouch). Masculinization occurs as a result of DHEA conversion to testosterone in fetal placenta and peripheral tissues. This results in too much masculinization in the female and insufficient masculinization in the male fetus. As with 21 $\alpha$ -hydroxylase deficiency, a spectrum of phenotypes exist, including classic salt-wasting, non-salt-wasting, and non-classic, late-onset forms.

Enzyme CYP17 (P450) catalyzes two reactions:

1. 17 $\alpha$ -hydroxylation of pregnenolone
2. 17, 20-lyase (side-chain cleavage) of 17-hydroxypregnenolone and 17-hydroxyprogesterone.<sup>6</sup>

This rare autosomal recessive disorder occurs in two forms: combined 17 $\alpha$ -hydroxylase and 17, 20-lyase deficiency (most common) and isolated 17, 20-lyase deficiency. Phenotypically, affected females have normal internal and external genitalia, but demonstrate sexual infantilism due to an inability of the ovaries to secrete estrogens at puberty. In both forms of the disorder, males display a developmental spectrum from a normal female phenotype to an ambiguous hypospadiac male. The magnitude of the decreased masculinization in the male infant correlates with the severity of the block in 17 $\alpha$ -hydroxylation. In mild defects, aldosterone secretion may be normal and hypertension absent.<sup>11</sup>

Also called lipid adrenal hyperplasia, StAR deficiency is a rare form of CAH and is the most severe genetic defect in steroidogenesis. It is associated with severe glucocorticoid and mineralocorticoid deficiency due to failure to convert cholesterol to pregnenolone.<sup>5,6</sup> Affected males have female external genitalia with a blind vaginal

pouch, while females demonstrate normal internal and external genitalia. Many patients die in infancy, while about 33% survive with replacement therapy. While 46XY patients have severe testosterone deficiencies, 46XX females can enter puberty and menstruate, although they later develop polycystic ovaries and progressive ovarian failure. No surviving 46XY patient has demonstrated testis function at puberty.

### *Gonadal dysgenesis*

Mixed gonadal dysgenesis is the next most common intersex disorder. In general, gonadal dysgenesis disorders comprise a spectrum of anomalies ranging from complete absence of gonadal development to delayed gonadal failure. Complete or partial gonadal dysgenesis includes failed gonadal development in genetic males and females due to abnormalities of sex or autosomal chromosomes. This involves a gonad that has not properly developed into a testis or an ovary such as a dysgenetic testis or a streak gonad.

Complete gonadal dysgenesis describes a 46XX child with streak gonads or, more commonly, a child with Turner's syndrome (45X or 45X/46XX). 45X/46XX mosaicism may be seen in up to 75% of patients with Turner's syndrome.<sup>12</sup> Another uncommon form of pure gonadal dysgenesis is called Swyer syndrome. The child looks female externally and has a uterus and fallopian tubes; however, the karyotype is 46XY with a Y chromosome that usually does not work and two dysgenetic gonads in the abdomen.<sup>13</sup>

Partial gonadal dysgenesis refers to disorders with partial testicular development, including mixed gonadal dysgenesis, dysgenetic male pseudohermaphroditism, and some forms of testicular or ovarian regression. Mixed or partial gonadal dysgenesis (45X/46XY or 46XY) involves a streak gonad on one side and a testis, often dysgenetic, on the other side. A patient with a Y chromosome in the karyotype is at a higher risk than the general population to develop a tumor in the streak or dysgenetic gonad. Gonadoblastoma is the most common tumor.<sup>14</sup> Although it is a benign growth, it can give rise to a malignant tumor called a dysgerminoma.<sup>15</sup> The risk of tumor is about 20–25% and is age-related. Surgical removal of the gonad is therefore recommended. The patient with a 45X/46XY karyotype and normal testis biopsy could retain his testis if it is scrotal or can be placed in the scrotum. This child would then need a very close followup of the testis, usually by monthly self-examination for tumor formation.

### *True hermaphroditism*

True hermaphroditism describes expression of both ovarian and testicular tissue in the individual. True hermaphroditism can result from sex chromosome mosaicism, chimerism, or a Y chromosome translocation. The most common karyotype in the United States is 46XX, although 46XY or mosaicism or chimerism (46XX/46XY) can occur. While a mosaicism may occur from a chromosomal nondisjunction, chimerism may result from a double fertilization (an X and a Y sperm) or from fusion of two fertilized eggs. Some patients with 46XX true hermaphroditism have the SRY gene translocated from the Y to the X chromosome. However, for most patients, the genes responsible are not yet identified.<sup>16,17</sup> This fairly uncommon condition can be further classified into three groups:

- lateral TH has a testis on one side and an ovary on the contralateral (usually left) side

- bilateral TH has an ovotestis on each side
- unilateral TH, which is the most common form, has an ovotestis on one side and either a testis or an ovary on the contralateral side.

The genital development in TH patients is ambiguous, with the phenotypic expression of hypospadias, cryptorchidism, and incomplete fusion of the labioscrotal folds. The genital duct differentiation in these patients generally follows that of the ipsilateral gonad on that side, such as a female fallopian tube with an ovary and a male vas deferens with a testis.<sup>18</sup>

### *Male pseudohermaphroditism*

Male pseudohermaphroditism is a heterogeneous disorder in which testes are present but the internal ducts system and/or the external genitalia are incompletely masculinized (Figure 62.3). The phenotype is variable and ranges from completely female external genitalia to mild male ambiguity such as hypospadias or cryptorchidism. Male pseudohermaphroditism can be classified into eight basic etiologic categories:



**Figure 62.3**

(A and B) 46XY patient with severe hypospadias and unilateral cryptorchidism due to dysgenetic male pseudohermaphroditism.

1. Leydig cell failure
2. testosterone biosynthesis defects
3. androgen insensitivity syndrome
4. 5 $\alpha$ -reductase deficiency
5. persistent müllerian duct syndrome
6. testicular dysgenesis
7. primary testicular failure or vanishing testes syndrome
8. exogenous insults.

### **Leydig cell failure**

Male pseudohermaphroditism can result from Leydig cell unresponsiveness to human chorionic gonadotropin (hCG) and luteinizing hormone (LH), since the production of testosterone by the Leydig cells is critical to male differentiation of the wolffian ducts and the external genitalia. The phenotypes of these patients vary from normal female to hypoplastic external male genitalia.

### **Testosterone biosynthesis enzyme defects**

Defects in four of the steps of the steroid biosynthetic pathway from cholesterol to testosterone may produce genital ambiguity in the male<sup>5,6</sup> (Figure 62.2). These include the less common forms of CAH:  $3\beta$ -HSD, GYP 17  $17\alpha$ -hydroxylase/17, 20-lyase), steroidogenic acute regulatory (StAR) protein deficiency, and  $17\beta$ -HSD deficiencies. Complete deficiency of  $3\beta$ -HSD impairs the synthesis of adrenal and cortisol and also gonadal testosterone and estradiol.<sup>19-21</sup> These newborns demonstrate severe CAH and exhibit signs of mineralocorticoid and glucocorticoid deficiency in the first week of life. Affected female infants have mild-to-moderate clitorimegaly. Male infants exhibit ambiguous genitalia with variable degrees of hypospadias, cryptorchidism, penoscrotal transposition, and a blind vaginal pouch. Masculinization occurs in these infants as a result of DHEA conversion to testosterone in the fetal placenta and peripheral tissues. This results in too much masculinization in a female and insufficient masculinization in the male fetus. Females with  $17\alpha$ -hydroxylase or 17, 20-lyase deficiency have normal internal and external genitalia but demonstrate sexual infantilism due to an inability of the ovaries to secrete estrogen at puberty. In both forms of the disorder, males display a developmental spectrum from the normal female phenotype to the ambiguous hypospadiac male.<sup>11,22</sup> Affected males with StAR deficiency have female external genitalia with a blind vaginal pouch, whereas females demonstrate normal internal and external genitalia.<sup>23,24</sup> The affected 46XY males with  $17\beta$ -HSD deficiency have external female genitalia, inguinal testes, internal male ducts, and a blind vaginal pouch. At puberty, these patients demonstrate an increase in their levels of gonadatropins, androstenedione, estrone, and testosterone. Delayed virilization may ensue if some testosterone levels approach the normal range.<sup>25,26</sup>

### **Androgen insensitivity syndrome**

The broad phenotypic spectrum of androgen sensitivity syndrome (AIS) includes 46XY patients that vary from normal female external genitalia that is seen in AIS7 or testicular feminization to normal males with infertility such as an AIS1. This disorder affects 1 in 20,000 live male births and the patients demonstrate a maternal inheritance pattern since the androgen receptor gene is located on the long arm of the X chromosome.<sup>27</sup> The amino terminal domain of the gene is encoded by exon 1 and is critical to target gene transcription regulation. Exons 2 and 3 encode the DNA-binding domain and the 5' region of exon 4 encodes the hinge region containing the nuclear targeting signal. The 3' region of exon 4 and exons 5–8 encodes the steroid-binding domain that confers ligand

specificity. Binding of dihydrotestosterone or testosterone to this receptor ligand-binding domain results in activation of the receptor.<sup>28</sup> The majority of androgen receptor gene mutations affect the steroid-binding domain and result in receptors unable to bind androgens or receptors that bind androgens but exhibit qualitative abnormalities and do not function well. Exons 5 and 7 are the sites of many of the point mutations and the distribution of these alterations is similar for patients with either complete or partial androgen resistance.<sup>29–31</sup>

A child with complete androgen insensitivity externally resembles a girl, although the karyotype is XY and testes are located internally. Traditionally, these children have been raised as girls. Most children are not diagnosed until a work-up is performed when primary amenorrhea occurs at puberty. Occasionally, this condition is also discovered at the time of inguinal hernia repair or, more recently, when a prenatal karyotype does not match the external phenotype of the newborn child (Figure 62.4). An interesting finding is the phenotypic variability of families with affected males with partial AIS. This suggests that other factors in the sex differentiation cascade influence the phenotypic manifestation of gene mutations.



**Figure 62.4**

Abdominal testis identified at time of inguinal hernia repair in 46XY patient with complete androgen insensitivity syndrome.

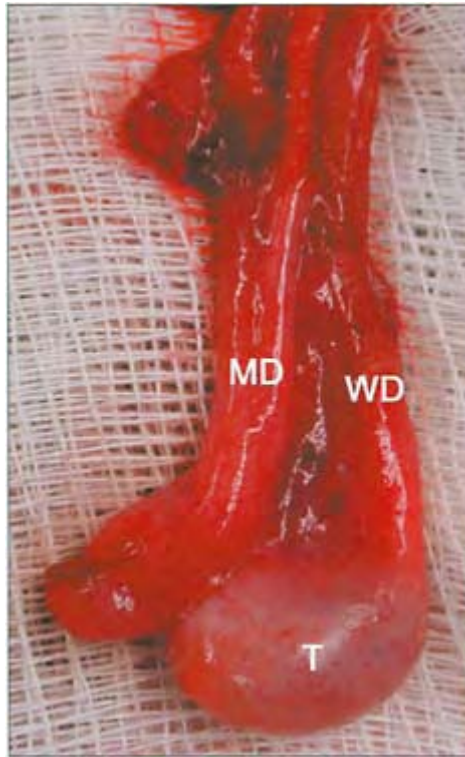
### **5 $\alpha$ -Reductase deficiency**

5 $\alpha$ -Reductase deficiency was first described by Nowakowski and Lenz in 1961 as pseudovaginal perineal scrotal hypospadias.<sup>32</sup> This is an autosomal recessive condition and these patients have a defect in the conversion of testosterone to its 5 $\alpha$ -reduced metabolite, di-hydrotestosterone (DHT). These patients have a 46XY karyotype and ambiguous external genitalia but normally differentiated testes with male internal ducts. However, at puberty, significant virilization occurs as testosterone levels increase into the adult male range while DHT remains disproportionately low. The SRD5A2 gene on

chromosome 2 accounts for most fetal 5 $\alpha$ -reductase activity. There are three genetic isolates of this disorder that have been described: they are found in the Dominican Republic, the New Guinea Samba Tribe, and in Turkey. Many of these patients undergo a change of their gender identity from female to male after puberty.<sup>33,34</sup> The patients with SRD5A2 gene deletions have measurable DHT levels at puberty, probably due to the peripheral conversion of testosterone to DHT. Virilization can be secondary to slightly increased plasma DHT levels and to the chronic effect of adult testosterone (T) levels on the androgen receptor.

### **Persistent müllerian duct syndrome**

Antimüllerian hormone (AMH), which is also termed müllerian inhibitory substance (MIS), is secreted by the Sertoli cells from the time of fetal seminiferous tubule differentiation until puberty. MIS binds to a receptor in the mesenchyme surrounding the müllerian ducts before 8 weeks gestation, causing apoptosis and regression of the müllerian duct.<sup>35</sup> The diagnosis of persistent müllerian duct syndrome is often made at the time of inguinal hernia repair or orchiopexy: hence the term *hernia uteri inguinale* (Figure 62.5). Persistent müllerian duct syndrome (PMDS) can occur from a failure of the testes to synthesize or secrete MIS due to an AMH gene mutation or from a defect in the response of the duct to MIS (AMH2 receptor mutation). PMDS is inherited in a sex-linked autosomal recessive manner and AMH mutations are most common in Mediterranean or Arab countries with high rates of consanguinity.<sup>36</sup> Most of these familial mutations are homozygous and the patients have low or undetectable levels of serum MIS. In contrast, AMH2 receptor mutations are often heterozygous and are more common in France and Northern Europe. These patients usually have high-normal or elevated MIS concentrations.<sup>12</sup>



**Figure 62.5**

Retained müllerian structures in 46XY patient with unilateral cryptorchidism and persistent müllerian duct syndrome (MD= Müllerian duct, WD=wolffian duct. T=testis).

### **Testicular dysgenesis**

Dysgenetic male pseudohermaphroditism or dysgenetic testes can result from mutations or deletions of any of the genes involved in the testis determination cascade. These patients with dysgenetic gonads exhibit ambiguous development of the internal genital ducts, the urogenital sinus, and the external genitalia. The SRY gene is a single exon gene located on the short arm of the Y chromosome near the pseudoautosomal region.<sup>37</sup> SRY gene mutations usually result in complete gonadal dysgenesis and sex reversal as seen in XY sex reversal, or Swyer syndrome. Histologic analysis of dysgenetic gonads of XY males revealed that those with normal SRY had some element of rete testis and tubular function, whereas those with SRY mutations had completely undifferentiated gonads similar to those of 45X or Turner's syndrome individuals. Thus, it is seen that SRY may



have a direct role in testicular formation in addition to its indirect role in initiating the male differentiation cascade. The DSS locus (*dosage* sensitive sex-reversal) has been mapped to the Xp21 region, which contains the DAX1 gene. Duplication of the DSS locus has been associated with dysgenetic MPH and other anomalies. The DSS locus has been theorized to contain a wolffian inhibitory factor, which acts as an inhibitory gene of the testis determination pathway.<sup>38</sup> Swain et al have shown that DAX1 antagonizes SRY action in mammalian sex determination.<sup>39</sup> Male patients with Denys-Drash syndrome have ambiguous genitalia with streak or dysgenetic gonads, progressive neuropathy, and Wilms' tumor. Analysis of these patients revealed heterozygous mutations of the Wilms' tumor suppressor gene (WT1) at 11p13.<sup>40</sup> The WAGR syndrome (Wilms' tumor, aniridia, genitourinary abnormalities, mental retardation) is also associated with WT1 alterations.<sup>41</sup> The genitourinary anomalies seen in the WAGR syndrome are usually less severe than in Denys-Drash syndrome. The SOX9 gene has been associated with campomelic dysplasia, an often lethal skeletal malformation with dysgenetic MPH.<sup>42</sup> Affected 46XY males have phenotypic variability from normal males to normal females, depending on the function of the gonads.

### **Congenital anorchia**

Congenital anorchia or vanishing testes syndrome encompasses a spectrum of anomalies resulting from cessation of testicular function.<sup>43</sup> A loss of testes prior to 8 weeks gestation results in 46XY patients with female external and internal genitalia and either no gonads or streak gonads. A loss of testes at 8–10 weeks in development leads to ambiguous genitalia and variable ductal development. A loss of testis function after the critical male differentiation period, which is at 12–14 weeks gestation, results in a normal male phenotype externally, along with anorchia internally (Figure 62.6). Both sporadic and familial forms of anorchia exist. The familial cases, including some reports of monozygotic twins, support the presence of an as-yet unidentified mutant gene in some patients with the syndrome.

### **Exogenous source**

Exogenous insults to normal male development include maternal ingestion of progesterone or estrogen or various environmental hazards. As early as 1942, Courrier and Jost<sup>44</sup> demonstrated an antiandrogen effect on the male fetus induced by a synthetic progestagen and, more recently, Silver et al<sup>45</sup> showed an increased incidence of hypospadias in male offspring conceived by in-vitro fertilization. They hypothesized that the increased risk may be secondary to maternal progesterone ingestion. Sharpe and Skakkebaek have further postulated that the increase in



**Figure 62.6**

Atretic gonadal vessels seen by laparoscopy in 46XY patient with congenital anorchia.

reproductive abnormalities in men is related to an increase in the in-utero exposure to environmental estrogens.<sup>46</sup>

#### *Sex chromosome anomalies*

Sex chromosome anomalies comprise another category of patients with intersexuality. Klinefelter's syndrome (47XXY) usually becomes evident during adolescence as the patient develops gynecomastia, variable androgen deficiency, and small atrophic testes with hyalinization of the seminiferous tubules. These patients demonstrate aspermatogenesis and increasing gonadotropin levels. 47XXY males may develop through nondisjunction of the sex chromosomes during the first or second meiotic division in either parent or, less commonly, through mitotic nondisjunction in the zygote at or after fertilization. These abnormalities almost always occur in parents with normal sex chromosomes. 46XY/47XXY mosaicism is the most common form of the Klinefelter variants. The mosaics, in general, manifest a much milder phenotype than classic Klinefelter patients. A differentiation of testes and a lack of ovarian development in these patients indicates that a single Y chromosome with SRY expression is enough for testis organogenesis and male sex differentiation in the presence of as many as four X chromosomes in some Klinefelter patients. These testes are not truly normal, however, since they are usually small and azoospermic. Although there are sporadic reports of paternity, most fertile Klinefelter individuals have had sex chromosome mosaicism.<sup>47-49</sup>

#### *Sex reversal*

Categories of 46XX sex reversal include classic XX male individuals with apparently normal phenotypes, nonclassic XX males with some degree of sexual ambiguity, and XX

true hermaphrodites.<sup>50</sup> Eighty to ninety percent of 46XX males result from an anomalous Y to X translocation involving the SRY gene during meiosis. In general, the greater amount of Y DNA present, the more masculinized the phenotype. Eight to twenty percent of XX males have no detectable Y sequences, including SRY. About 1 in 20,000 phenotypic males have a 46XX karyotype. Most of these patients have ambiguous genitalia, but reports of classic XX males without the SRY gene do exist.<sup>38,50,51</sup> This phenomenon again raises the possibility of mutation of a downstream wolffian inhibitory factor when cases of normal masculinization are seen without the presence of the SRY gene.

### *History and physical examination*

Patient history should include the level of prematurity; ingestion of exogenous maternal hormones, such as those used in assisted reproductive techniques, and maternal use of oral contraceptives during pregnancy. A family history is also useful for any urologic abnormalities, neonatal deaths, precocious puberty, infertility, or consanguinity. Any abnormal masculinization or cushingoid appearance of the child's mother should also be noted. Abnormalities of the prenatal maternal ultrasound are also helpful, such as discordance of the fetal karyotype with the genitalia by sonogram (Figure 62.7).

On physical examination, one should note any phic features, including a short broad neck or widely spaced nipples. The patient should be examined in a warm



**Figure 62.7**

Prenatal ultrasound in 45X fetus showing discordant (male) genitalia (arrow).

room supine in the frog leg position with both legs free. An abnormal phallic size should be documented by width and stretched length measurements. One should describe the position of the urethral meatus and the amount of chordee (ventral curvature) and note the number of orifices: 3 in normal girls (urethra, vagina, and anus) or 2 in boys (urethra, anus). A rectal examination should also be performed for palpation of a uterus. With warmed hands, one should begin the inguinal examination at the anterior superior iliac

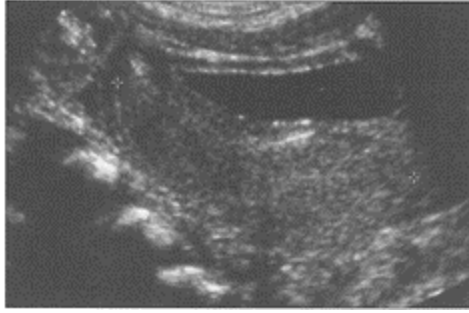
crest and sweep the groin from lateral to medial with a nondominant hand. Once a gonad is palpated, grasp it with the dominant hand and continue to sweep toward the scrotum with the other hand to attempt to bring the gonad to the scrotum. Occasionally, some soap or lubricant on the fingertips may aid in this examination. It is important to check size, location, and texture of both gonads if palpable. The undescended testis may be found in the inguinal canal, the superficial inguinal pouch, at the upper scrotum, or rarely in the femoral, perineal, or contralateral scrotal regions. One should also note the development and pigmentation of the labioscrotal folds along with any other congenital anomalies of other body systems.

For differential diagnosis and treatment purposes, the distinction needs to be made whether or not the gonad is palpable. Unless associated with a patent processus vaginalis, ovaries and streak gonads do not descend while testes and rarely an ovotestis may be palpable. If no gonads are palpable, all four categories are possible (FPH, MPH, GD, and TH). Of these, FPH is most commonly seen, followed by MGD. If one gonad is palpable, FPH and PGD are ruled out, while MGD, TH, and MPH remain possibilities. If two gonads are palpable, MPH and rarely TH are the most likely diagnoses. In 46XY boys, hypospadias and cryptorchidism without an underlying intersex etiology would be a diagnosis of exclusion after a full evaluation.

### *Patient evaluation*

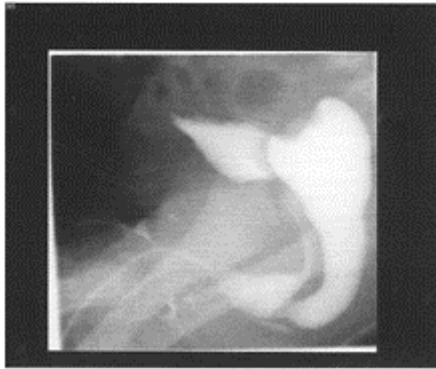
All patients require laboratory evaluation by serum electrolytes, 17-hydroxyprogesterone, testosterone, LH, and follicle-stimulating hormone (FSH) levels. A karyotype is also immediately performed. If the 17-hydroxyprogesterone level is elevated, 11-deoxycortisol and deoxycorticosterone levels will help differentiate 21 $\alpha$ -hydroxylase deficiency from 11 $\beta$ -hydroxylase deficiency. If the 17-hydroxyprogesterone level is normal, a testosterone to DHT ratio, along with androgen precursors before and after hCG stimulation, will help elucidate the MPH etiology. During the first 60–90 days of life, there is a normal gonadotropic surge, with a resultant increase in the testosterone level of the infant. During this specific time period, one can forego the hCG stimulation for the androgen evaluation. A failure to respond to hCG, in combination with elevated LH and FSH levels, is consistent with anorchia.

An ultrasound can detect gonads in the inguinal region, where they are also most easily palpable, but it is only 50% accurate in showing intra-abdominal testes (Figure 62.8). A computed tomography (CT) scan and a magnetic resonance imaging (MRI) scan may also help to delineate the anatomy, although they are more expensive. These tests are also helpful in identifying a uterus. A genitogram should be performed to evaluate a urogenital sinus, including the entry of the urethra in the vagina. A cervical impression can be identified on the vaginogram<sup>52</sup> (Figure 62.9). Infants in whom TH, MGD, or MPH is considered will require an open or laparoscopic exploration with bilateral deep longitudinal gonadal biopsies for histologic evaluation.



**Figure 62.8**

Postnatal ultrasound showing large uterus filled with debris (between cursors) behind the bladder.



**Figure 62.9**

Genitogram showing superior cervical impression in vagina emptying into a urogenital sinus.

### **Treatment options and indications**

Much current research is aimed at understanding the influence of androgens on the fetal and newborn brain and its relationship to gender identity. Diagnosis and management of these children is very individualized and should always involve a team approach, which includes the pediatric urologist, endocrinologist, geneticist, and the child's parents immediately after birth.

*Female pseudohermaphroditism*

Treatment of the newborn with CAH involves the correction of dehydration and salt loss by electrolyte and fluid therapy with mineralocorticoid replacement.<sup>4</sup> Glucocorticoid replacement is then generally added upon confirmation of the diagnosis. Infants that are going to be raised as girls usually undergo clitoral reduction and vulvovaginoplasty in early infancy, but controversy exists on the timing of surgery and all aspects must be weighed prior to decision making. Surgery can be performed for an infant, toddler, or adolescent. Many surgeons advocate early surgery for both technical and psychologic reasons, realizing that vaginal revision may be needed after puberty. Surgery has three main aims:

- reducing the size of the enlarged masculinized clitoris
- reconstructing the female labia
- increasing the opening and possibly length of the vagina.

These procedures have gone through many changes during the history of surgery. Surgical technique continues to be revised to optimize the girl's external appearance and functional size, while maintaining adequate sensation. Clitorectomy, which involves removing the entire clitoris, is long out of practice, as is clitoral recession without reduction, since it is associated with painful erections upon stimulation. Reduction clitoroplasty is the operation of choice for most infants with clitorimegaly. The central portions of the corporal bodies are excised and the surgeon preserves the dorsal neurovascular bundles by incising Buck's fascia laterally at the 3 o'clock and 9 o'clock positions. The corporal bodies need to be dissected beyond the bifurcation to the inferior pubic rami, where they are transected. The remaining proximal and distal portions of the bodies are then reapproximated and placed in the investing fascia: this optimizes future erectile function. Occasionally, a glansplasty is required for an extremely large glans and this is accomplished by excising a triangle of tissue on the dorsum of the glans. A vulvoplasty is carried out by extending the incision for the clitoroplasty on either side of the midline strip of tissue down to the level of the vaginal orifice. Redundant labial scrotal skin is brought down as preputial flaps to form the labia minora.<sup>53-58</sup>

The position of the vagina should be accurately determined preoperatively by the genitogram as part of the work-up for intersex. There are four main types of vaginal repair:

- a simple cutback of the perineum
- a flap vaginoplasty
- a pull-through vaginoplasty
- a more extensive rotation of skin flaps or segmental bowel interposition.

Usually, a low vaginoplasty can be performed at the same time as the clitoroplasty. When the vagina opens very low, a simple cutback with a vertical midline incision may be all that is needed to open the introitus. Usually, however, a posterior based U-shaped flap is necessary for a tension-free anastomosis, reducing the risks of postoperative vaginal stenosis.<sup>53</sup> Exposure of the high vagina requires either a perineal approach (Hendren operation, Passerini-Glazel operation), a posterior vaginoplasty as recommended by Pena, or an anterior sagittal transanorectal vaginoplasty as described by Domini. When the

vagina is extremely high and small, replacement with a bowel segment will be necessary, usually with the sigmoid colon.<sup>57–60</sup>

### *Gonadal dysgenesis*

A streak gonad does not descend but it may be palpable as a small remnant of tissue in an inguinal hernia sac. If the testis is in the inguinal position, it can be removed using an incision in the groin, as for a traditional orchiopexy or hernia repair. If the gonad is in the abdomen, as is usually the case with the gonadal dysgenesis, then the treatment options include open abdominal exploration and removal of the gonads or laparoscopic gonadectomy, which is the usual preference. When a purely female anatomy exists, such as in Turner's syndrome or Swyer syndrome, no treatment may be necessary. These girls have sexual infantilism at puberty marked by no onset of secondary sexual development. Some degree of female development, however, may be seen in up to 20–25%. Since gonadoblastoma does not occur in the absence of Y chromosome material, removal of the streak gonads is not required.<sup>14</sup> Growth hormone is usually recommended early in childhood and estrogen therapy is begun after puberty to optimize the patient's height. Rare cases of spontaneous pregnancy have been reported, although infertility is the norm. Pregnancy may thus be possible using donor eggs and assisted reproductive techniques.

### *True hermaphroditism*

Generally, a female sex has been assigned to most patients due to the presence of a vagina, uterus, and ovarian tissue. Less commonly, the patient has a 46XY karyotype with adequate penile development and without a uterus present, so a male sex assignment would be more appropriate. The decision of sex of rearing should always be deferred until the child has had an adequate evaluation of his genitourinary system. Usually, the internal organs need to be visualized and the gonads biopsied. This can be done through an open abdominal exploration or accomplished with the use of the laparoscope. If raised as a female, the child should have dysgenetic testicular tissue removed due to the risk of malignancy. The possible need for vaginoplasty can be performed early or deferred until puberty. If the child is raised as a boy, he should have any hypospadias or cryptorchidism repaired as an infant. Testosterone supplementation may be needed if the amount of testicular tissue present is inadequate to begin or continue puberty. A persistent müllerian duct, such as a uterus and fallopian tubes, has usually not fully regressed and connects to the urethra near the bladder at the verumontanum. If there is a decision to rear the child as a boy, the structures are generally removed, taking care not to injure the vas deferens, which usually runs alongside the uterus. Extensive dissection behind the bladder neck and up to the area where the müllerian structures insert into the urethra is usually contraindicated in order to avoid damage to the sphincter mechanism, risking incontinence. Both open and laparoscopic excisions have been reported.<sup>61–63</sup> Arguments for removal of the müllerian structures include the possibility of cyclic hematuria post puberty, or the formation of stones or chronic urinary tract infections if the continuity with the urethra is maintained and stasis occurs in a dilated müllerian remnant.<sup>61–64</sup> Arguments against removal maintain that complications from the structures are

uncommon and their removal risks injury to the vas deferens, the bladder neck, and the urethral sphincter.<sup>65</sup>

### *Male pseudohermaphroditism*

Decreased masculinization (hypospadias with cryptorchidism or more ambiguous development) is seen in most patients with MPH. In untreated patients with 5 $\alpha$ -reductase deficiency, significant virilization occurs at puberty, as testosterone levels increase into the adult male range while DHT remains disproportionately low. Treatment is currently unclear for this enzyme deficiency when diagnosed in infancy. Male gender assignment has been recommended because the natural history of this deficiency is virilization at puberty with subsequent change to male gender. However, this decision requires surgical hypospadias repair and orchiopexy with male hormonal replacement.

Rarely do patients with dysgenetic testes have fully masculinized external genitalia. The surgical issues are very dependent on the degree of masculinization in each individual case, which also influences the decision process of sex assignment. If a 46XY infant with testicular dysgenesis is going to be raised as a male, he will need a hypospadias repair, orchiopexy, or possibly orchiectomy. Müllerian ducts have usually not fully regressed and may be fully or partially removed at the time of other repairs in order to facilitate orchiopexies. As previously discussed, retained female structures have the potential for urinary tract infections, stones, or even cyclic hematuria at puberty. Dysgenetic testes may appear normal grossly but microscopically are disorganized and poorly formed; thus, a biopsy of the gonad is recommended in most children undergoing intersex evaluation. Currently, the recommendation is to remove an undescended dysgenetic testis because of the risk of malignancy.<sup>66,67</sup> In 45X/46XY patients, if the biopsy is normal and the testis is scrotal or can be placed in the scrotum, it should not be removed, but a risk of malignancy correlates with the extent of testicular descent. Tumors have also been reported in scrotal dysgenetic testes. A scrotal testis needs to be followed very closely for this reason. The possibility does exist of a male gender in these patients who would require a hypospadias repair yet would have removal of severely dysgenetic testis requiring replacement hormones. It would seem obvious that treatment in these cases needs to be individualized. The child's parents should discuss with the pediatric urologist, endocrinologist, geneticist, and psychiatrist the issues of testosterone imprinting in utero, the need for hormones pre- and postpuberty, the degree of masculinization, the function of the testis, and the extent of surgery that is required.

Affected boys with errors in testosterone production are undermasculinized, with varied degrees of hypospadias, cryptorchidism, bifid scrotum, or a blind vaginal pouch. For the patient reared as a boy, testosterone therapy may be indicated to augment penile size and to aid in the hypospadias repair. The natural history in some of these patients when untreated is virilization at puberty with a gender role change from female to male.<sup>25,26,68,69</sup> Therefore, many recommend a male gender assignment diagnosis. Some enzyme deficiencies require glucocorticoid and mineralocorticoid replacement and all of these patients need testosterone replacement at puberty for masculinization. Gonadectomy is required in 46XY patients raised as girls in order to address the risk of tumor formation in the future.



Traditionally, a child with a complete androgen insensitivity syndrome would be raised as a girl. Most of these children are not diagnosed until a work-up is performed when amenorrhea occurs at puberty. Occasionally, it is discovered at the time of inguinal hernia repair and more recently when a prenatal karyotype does not match the external phenotype of the newborn child. If the child is to be raised female, an orchiectomy is required. The testes are at risk for cancer development and the incidence of malignant tumors is estimated to be 5–10%.<sup>70,71</sup> Seminoma is the most common tumor seen, but nonseminomatous germ cell tumors and other malignancies have also been reported. Tumor risk appears to be greater in older patients and in those with complete rather than partial AIS, and tumor formation appears to occur postpuberty. Intratubular germ cell neoplasia has been identified in prepubertal boys with partial AIS but not complete AIS.<sup>71</sup> If an AIS patient presents with an inguinal hernia, the gonads are usually removed during the hernia repair for diagnosis and cancer risks. Vaginal dilation or vaginal augmentation may or may not be needed: usually this is reserved until after puberty and a number of techniques are available. In patients with partial AIS, orchiectomy is recommended as soon as the diagnosis is made to avoid further virilization in patients who will be raised in the female gender. Male gender assignment is usually successful in patients with a predominantly male phenotype; however, predicting the adequacy of masculinization in adulthood may not be possible based on the maternal family history or characterization of the androgen receptor genetic defect. Some children respond well to high-dose androgen therapy, but its durability is not yet clear.

Controversy exists concerning the best time to perform the orchiectomy. Traditionally, in an infant with complete AIS, the testes are left in place until after puberty to take advantage of the hormonal function and, in this way, natural female pubertal changes can occur by testosterone conversion to estrogen. After puberty is completed, the testes would be removed and replacement estrogen begun. Risks with this approach are as follows: no cancers have been reported in prepubertal children, but carcinoma-in-situ has been uncommonly seen. If the testes happen to be in the inguinal region, they can be easily injured. One also needs to explain to a mature postpubertal patient of the need to remove the testes. Of course, delaying the surgery also further increases the risks of testis cancer if the patient is lost to follow-up care. If orchiectomy is performed early, replacement hormones are then required for pubertal changes.

### **Patient and preoperative preparation**

Gonadectomy or orchiectomy is performed due to the malignant potential for patients assigned to female gender. If the patient is to be assigned a male gender and the gonads consist of testicular elements, they can be preserved and orchiopexies performed early. As previously discussed, an early prophylactic orchiectomy can be performed if patients are to be raised as female rather than undergoing a therapeutic orchiectomy after puberty. Inappropriate müllerian structures in males should be removed if needed to aid in orchiopexy or if needed for cyclic hematuria or urinary stones. Laparoscopy has been very useful both as a diagnostic and therapeutic procedure in boys with nonpalpable gonads. In the cases of intersex, laparoscopy is also helpful in defining the internal duct structures, removing structures contrary to the current gender assignment, helping in

gonadal biopsies, or removing gonads with an increased malignant potential. However, open laparotomy through a Pfannenstiel incision is better suited for deep longitudinal gonadal biopsies, which are generally preferred over a superficial forceps biopsy that would be used laparoscopically. Open laparotomy also facilitates a partial gonadectomy, which may be performed in cases of true hermaphroditism.

In general, diagnostic laparoscopy or a laparoscopic orchiopexy and laparoscopic gonadectomy are performed on an outpatient basis under general anesthesia. The child is placed supine with the arms tucked on the sides. The child is secured to the table in order to allow the table to be adjusted into the Trendelenburg position as needed. The position and draping of the child are suitable for an open abdominal procedure if this becomes necessary. A urethral catheter is inserted and left in for the entire case. An orogastric tube is used to decompress the stomach and we generally advise our anesthesiologist to avoid nitrous oxide in order to limit the potential for dilation of the bowel.

### **Recommended equipment or instruments**

I generally use a 5 mm lens system for most laparoscopic procedures. However, a 3 mm lens system provides adequate visualization for simple diagnostic laparoscopy. There is a greater assortment of 5 mm instruments available at this time, but as the mini-laparoscopic systems improve, most centers will probably convert to 3 mm working ports. The instrument that is most used is a 5 mm atraumatic grasper. Cautery is used sparingly during a laparoscopic orchiopexy since coagulation within 2 mm of a vessel can injure the vessel wall, possibly leading to thrombosis. A 5 mm vascular clip applier is used through the 5 mm cannulas. At this point 3 mm clipping devices are not commonly available. Laparoscopic scissors that may be used with or without cautery are also necessary. If one prefers to bring a testicle down into the scrotum through a 10 mm cannula, then this should be available as well as the previously mentioned 5 mm ports. Some centers also use Amplatz dilators to enlarge the scrotal canal for an orchiopexy.

### **Approach and helpful tips**

Cystoscopy will help elucidate a müllerian remnant entering the urethra. Catheterization of the verumontanum and injection of contrast can highlight the retained structures (Figure 62.10). If there is a history of chronic urinary infection, cystoscopy and basket stone extraction from the müllerian remnant can be performed (Figure 62.11).

Initial laparoscopic access is usually achieved at the infraumbilical position. However, some surgeons prefer the supraumbilical incision to avoid the umbilical vessels during open trocar placement. After incising the skin, the subcuticular tissues are spread, exposing the fascia, which is tagged with sutures and then incised. The peritoneum is identified and opened and a 5 mm insufflation port is then placed into the abdomen; 3 mm instruments are placed with cannulas, which resemble large Veress needles—thus, one does not use open access for placement of the 3 mm cannula. Open trocar placement is seen as the safest method of entering the abdomen in small children and minimizes complications of placement of a Veress needle into the bowel or major blood vessels.

The peritoneal cavity can be inspected with the lens attached to the camera prior to insufflation to ensure that the cannula placement is correct. Once an adequate pneumoperitoneum is achieved through insufflation, the surgeon takes note of all vessels, vas deferens, intraabdominal gonads, and presence of any müllerian structures. If a patent processus vaginalis is noted, pressure on the inguinal canal can push peeping testes back into the abdomen for visualization. If the internal inguinal ring is closed, the surgeon examines for a blind-ending vas deferens close to blind-ending spermatic vessels. The finding of a blind-ending vas deferens alone does not prove a testis has vanished and further laparoscopic exploration is needed up to the origin of the gonadal vessels near the kidneys. A high abdominal testis can be either removed or brought down to the scrotum in a primary or staged fashion. Correct placement of the laparoscopic ports is important. The camera port is generally in the infraumbilical incision. This may be all that is needed for a diagnostic laparoscopy. However, further procedures generally require placement of two other working ports. These working ports are placed at the midclavicular line just below or even with the umbilicus. To work on the right inguinal region, the left lower quadrant port is generally placed slightly lower and vice versa for the left side. However, in cases of intersex, work may be done on both sides and both ports can be placed slightly below the umbilicus in the midclavicular line on the right and left sides. In very small children, it is helpful to place the working ports above the level of the umbilicus in order to avoid crossing the instruments and to facilitate their use.

The surgeon stands on the side opposite to the undescended testis or gonad in question. The child is placed in a mild Trendelenburg position with the lateral tilt away from the side that is being examined. A laparoscopic incision with scissors is made on the anterior lip of the patent processus vaginalis and continued laterally.<sup>72</sup> This incision is then carried medially to the adjacent gonadal vessels. The incision from the anterior lip is continued medially and extended further along the path of the vas deferens with care to leave a wide strip in order to preserve the paravasal vasculature. Elevating the gonadal vessels by grasping the local tissue or gonad with atraumatic



**Figure 62.10**

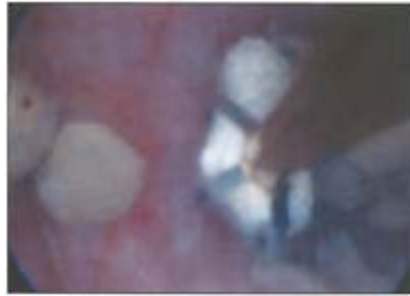
(A and B) Cystoscopic catheterization of utricular opening in urethra (A) and

## contrast study demonstrating uterus and right fallopian tube (B).

grasping forceps allows for further dissection distally along the sac of a patent processus vaginalis if present. This is especially helpful in a peeping or high inguinal testis. The gonadal vessels are on the medial posterior aspect of the hernia sac. With an undescended testis, care must be taken to define a caudal extent of the vas deferens if there is a long looping vas. Since gubernacular attachments are very vascular, they are divided with cautery. Incision in the peritoneum is extended laterally along the gonadal vessels toward the kidney. Further dissection along the medial aspect of the vas deferens creates a triangular flap of peritoneum containing the juncture of the vas gonadal vessels and testis. When the testis has been sufficiently mobilized, it can then be prepared for orchiopexy into the scrotum or removal in cases of AIS. For gonadectomy, 5 mm vascular clips are placed on the gonadal vessels proximal to the gonad. A similar clip is placed on the vas deferens. If a staged orchiopexy is needed, a clip can be placed on the gonadal vessels as far rostral as possible, allowing for a communication between the arteries of the vas deferens and the most distal spermatic vessels to increase over the next 6 months. Koff and Sephic, however, suggest that the communication between the caudal spermatic vessels and the arteries to the vas occur within the testes or close to the testicular hilum.<sup>73</sup> They therefore recommend placing the clip close to the testes in order to improve the mechanics of transfer provided by division of the spermatic vessels.

For relocation of the testis to the hemiscrotum, a small transverse incision is created on the hemiscrotum and a subdartos pouch is dissected. We use a 5 mm port advanced through the hemiscrotum and pass it into the peritoneal cavity medial to the medial umbilical ligament but lateral to the bladder. Some centers employ graspers through the 5 mm port, others change over to a 10 mm cannula, and yet others simply advance a hemostat into the peritoneal cavity in order to grasp the testis and bring it down to the scrotum where it is anchored in place. In the small child, all cannula sites are closed, including 3 mm or 5 mm sites, since a cannula site omental herniation has been described in a 3.5 mm cannula site in an infant. The umbilical cannula site is closed after all carbon dioxide has been removed from the abdomen.

Various laparoscopic techniques have been described for intersex procedures. Laparoscopic gonadectomy, as previously described, has become our standard approach for 46XY AIS patients who have complete testicular feminization and also in cases of 46XY Swyer syndrome or gonadal dysgenesis with the Y component in a mosaic karyotype in order to prevent gonadal tumor formation (Figure 62.12). These techniques have been reported by many institutions.<sup>74-76</sup> Cystoscopy for complete AIS reveals a blind-ending vaginal pouch without a cervix, and laparoscopy



**Figure 62.11**

Cystoscopy of large utricle with basket stone extraction.

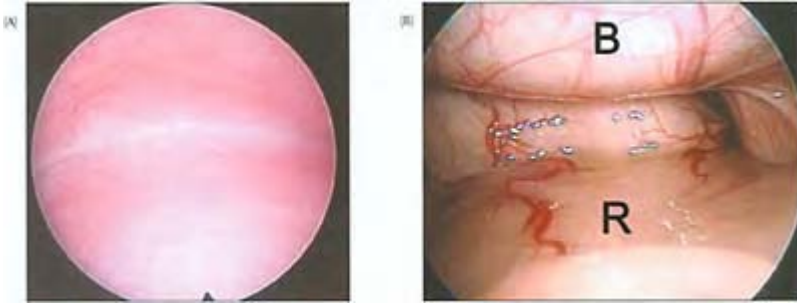


**Figure 62.12**

Laparoscopic orchiectomy of abdominal testis in 46XY patient with complete androgen insensitivity syndrome.

for gonadectomy shows absence of the cervix behind the bladder (Figure 62.13).

For true hermaphroditism, we prefer to convert a diagnostic laparoscopy to open gonadal biopsy in order to obtain a deep longitudinal gonadal biopsy. In most ovotestes, a polar distribution is seen with a clear demarcation between the two components. Rarely, however, the gonad may contain an outer ovarian cortex with an inner



**Figure 62.13**

46XY patient complete androgen insensitivity syndrome: vaginostomy (A) showing absence of cervix and laparoscopy (B) showing absence of uterus between the bladder (B) and rectum (R).

medullary zone of testicular tissue, which might be missed with a simple laparoscopic forceps biopsy, although this technique has been described<sup>61,65,77</sup> (Figure 62.14). In cases of retained müllerian structures, such as in PMDS, a hysterectomy can be performed by dissection of the hypoplastic uterus in the medial confluence of the streak gonads behind the bladder without sectioning of the wolffian ductal structures. Lateral to the uterine body, there are blood vessels that need to be cauterized. After incision of the peritoneal cul-de-sac, distal dissection of the uterus can be performed in the retrovesical space. The bladder facilitates this process. To remove all of the components, traction on the uterus enables the entire gonad duct and uterus complex to be removed en bloc.<sup>61</sup> Completion of this dissection usually requires removal through a 10 mm trocar. In cases of PMDS, however, the undescended testes need to be relocated to the scrotum. Extreme care must be taken when dissecting along the lateral edges of the uterine body, since this is where the vas deferens runs and injury may occur. It must be noted, however, that there are also some areas of vasal atresia in cases of PMDS. We may simply remove as much of the uterine body as needed in order to facilitate the orchiopexy. In contrast, others have simply bivalved the uterine body in the middle in order to allow both testes to reach the scrotum without tension (Figure 62.15). Various laparoscopic treatment options for orchiopexy with retained müllerian structures employing laparoscopic, laparoscopic assisted, or open methods through a Pfannenstiel incision have also been described. Ng and Koh describe three laparoscopic treatment options—division of the vas and oviduct and ipsilateral orchiopexy; division of spermatic vessels, followed

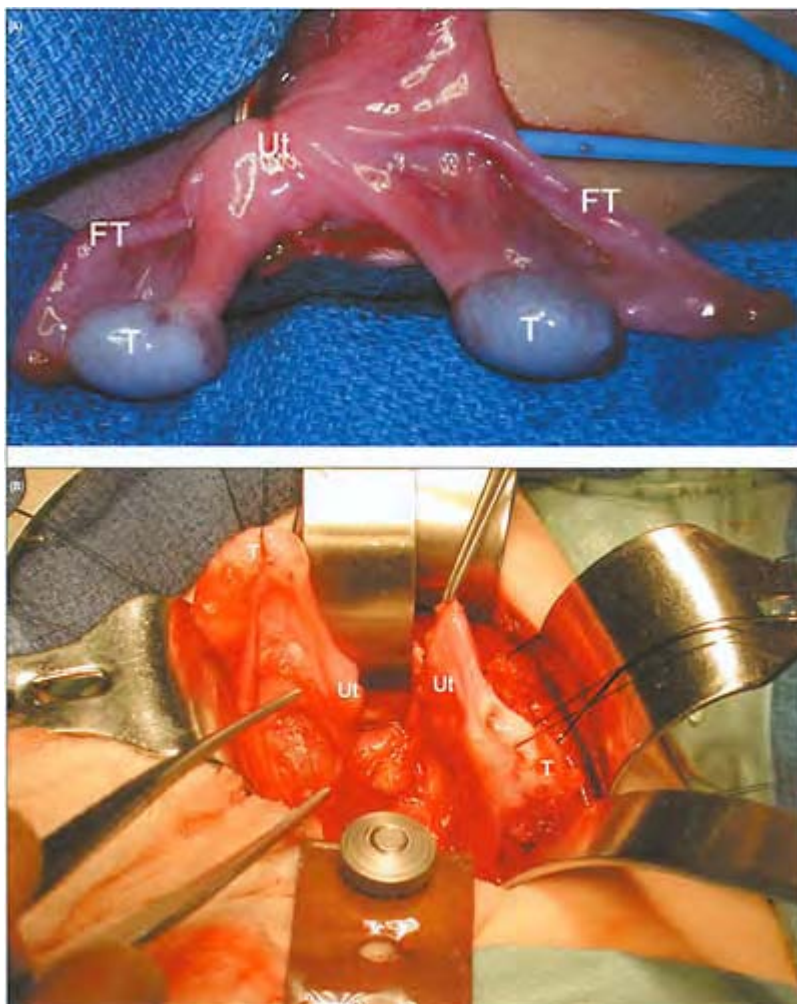


**Figure 62.14**

Laparoscopic biopsy of abdominal gonad.

later by Ombrédanne operation; and a one-stage division of spermatic vessels and Ombrédanne operation.<sup>78</sup>

Vaginal agenesis is found as part of the Mayer—Rokitansky-Küster-Hauser syndrome and laparoscopic techniques for creation of a neovagina have been reported by a number of authors.<sup>79,80</sup> A neovagina might also be required in severe cases of 46XX CAH and other cases of severe genital ambiguity without formation of any female structures. The Vecchietti procedure for creation of a neovagina was described for treatment of Rokitansky-Küster-Hauser syndrome in 1970 and has since been referred by many through both laparoscopic and open techniques.<sup>79</sup> Chabre et al described a bilateral laparoscopic adrenalectomy for CAH in an adult with severe hypertension. This patient had two novel mutations in



**Figure 62.15**

(A and B) 46XY patient with persistent müllerian duct syndrome (A) and open bivalve of uterus to enable orchiopexies of bilateral abdominal testes (Ut=uterus, FT=fallopian tube, T=testis).

the splice donor sites of the CYP11B1 gene. The surgery was followed by normalization of blood pressure and good compliance with a glucocorticoid and androgen substitution therapies.<sup>81</sup>



### **Common and unusual intraoperative and acute postoperative problems**

The most common initial difficulty encountered with Veress needle is improper placement, resulting in injuries to the stomach, bowel, bladder, and major vessels.<sup>82</sup> Very thin patients, infants, and adolescents are at particular risk of vascular injuries, since there is less distance between the anterior abdominal wall and the great vessels. In adults, the site of injury should be re-examined during and at the end of the laparoscopic procedure. Usually in children, and if there is any question regarding the injury, an immediate open laparotomy is performed and the perforation examined directly and repaired.

Carbon dioxide is the preferred agent for insufflation because it is readily available and inexpensive, suppresses combustion with cautery and lasers, and is rapidly absorbed. However, this absorption across the peritoneum may result in hypercarbia and acidosis. One disadvantage of carbon dioxide is that it may make the patient more prone to cardiac arrhythmias compared with other agents such as nitrous oxide. Nitrous oxide, however, is highly combustible and is insoluble in the blood. If it is directly injected into the bloodstream, serious embolism will occur. Pneumoperitoneum also exerts compression upon the vena cava, which may hinder cardiac return. Gas emboli, as previously described from CO<sub>2</sub> entering venous channels that are exposed during an operative dissection, can be fatal unless detected rapidly.

On placement of the Veress needle, if the angle of the needle is too oblique, it may slide down along the peritoneum without actually penetrating the peritoneum. Insufflation will then occur between the fascia and the peritoneum, with expansion of the preperitoneal space. Reinsertion of the Veress needle is required or one can convert to the open Hasson technique. One clue would be an elevated reading through the insufflation port (above 15 mmHg), since the carbon dioxide is being pumped into a closed space. Insufflated gas may also dissect along the extraperitoneal fascial planes and into the thoracic or pelvic regions, resulting in subcutaneous or scrotal emphysema or pneumomediastinum. This is not a serious problem and is easily diagnosed by palpating crepitus. Symptomatic pneumomediastinum or pneumothorax requires immediate termination of the procedure, evacuation of the peritoneal gas, and possibly further treatment with a tube thoracostomy. When performing procedures with a patent processus vaginalis, it is a good routine to manually compress the scrotum at the end of the procedure in order to release the pneumoscrotum.

Unlike injuries with the Veress needle, placement of a trocar into the intestinal tract, bladder, or a major blood vessel requires immediate open laparotomy and repair. The trocar and its sheath should be left in place while opening the abdomen in order to minimize bleeding or intestinal contamination and also to help identify the site of injury. An exploration for an abdominal gonad or extended dissection of gonadal vessels may place the ureter at risk especially near the beginning of the external iliac vein where the ureter crosses the bifurcation of the iliac artery. Development of gross hematuria or pneumaturia during a laparoscopic procedure usually suggests a bladder injury. Intravenous administration of methylene blue or indigo carmine can help identify a ureteral injury or placement of the dye into the bladder through a Foley catheter can help identify a bladder injury when the area is examined laparoscopically. Cystoscopy and

retrograde ureterograms may be required. The ureter may be stented or directly repaired if needed. Minor bladder injuries usually require only Foley catheter drainage.<sup>82,83</sup>

In reconstructive surgery for CAH, a decrease in sensation to the clitoris may result despite microsurgical handling of the neurovascular supply. Urethral stricture or diverticulum formation have also been described, as in a male hypospadias repair.<sup>84,85</sup> Although uncommon, narrowing of the vaginal opening may develop from scar, and injury to the rectum or colon has also been described. As surgical techniques improve, so do outcomes. In each case, the repair is individualized and agreed upon only after extensive counseling by all physicians involved. The discussion with the family should include a full description of the current anatomy, the timing and types of surgery, the need for further treatment, and expectations after the repair.

All infants raised as boys will require a hypospadias repair and chordee correction. Most repairs are one-stage procedures, however, some severe cases may be performed by a two-stage urethroplasty. Orchiopexies are usually carried out at the same time as the hypospadias repair.

## Results

Although many of the procedures from 20 years ago are outdated and techniques have changed, long-term results of intersex surgery are scarce. No long-term results of infant reduction clitoroplasty are available. Gearhart et al studied patients who underwent reduction clitoroplasty with preservation of a dorsal neurovascular bundle and found that elicitation of evoked potentials was well preserved.<sup>86</sup> This confirms that the neurologic pathways are intact; however, it does not prove normal erotic sensation. Since sexual fulfillment is a complex subject that involves not only clitoral and vaginal sensation but also psychological factors, these mechanisms are still not fully understood.<sup>86,87</sup> Some women who have had a clitorrectomy as infants have still been capable of orgasm, and approximately 20% of adult women who have never had any genital surgery are anorgasmic.

The most common complication after vaginoplasty is vaginal stenosis. An examination under anesthesia should be performed prior to puberty to ensure that normal menstruation can occur without obstruction. Adequate caliber for intercourse can usually be obtained by self serial dilation during late adolescence. Current available data suggest that many of the patients who undergo early vaginoplasty will need some sort of revision for stenosis of the introitus later in life.

Success rates for inguinal orchiopexy are 87–92%, with the higher rates for children less than 6 years old. Success rates for abdominal orchiopexies are slightly less, 74–82%.<sup>88</sup> Inadequate testis position occurs in up to 10% of cases and testicular atrophy is seen in about 5%. Damage to the vas deferens occurs in 1–2% and epididymo-orchitis is uncommon. Baker et al described a multi-institutional analysis of laparoscopic orchiopexy.<sup>89</sup> Using information from 10 institutions, they noted a 15% loss to follow-up rate. Success rates included 97.2% for primary laparoscopic orchiopexy without vessel division, 74.1% for single-stage laparoscopic orchiopexy with division of the spermatic vessels, and 87.9% for a two-stage laparoscopic orchiopexy with a first-stage division of the vessels. There was an overall 92.8% success rate for laparoscopic surgery. This is

higher than that historically ascribed to open orchiopexy. Single-stage laparoscopic orchiopexy with division of the vessels had a markedly higher atrophy rate than two-stage laparoscopic orchiopexy.

A successful hypospadias repair gives the patient a straight penis with a urethra at the end that allows the boy to stand to urinate and direct his urinary stream. After puberty, it also provides for an erect penis which will be sensitive and straight enough for adequate intercourse while allowing a forward deposit of semen with ejaculation. The two main complications of hypospadias surgery are urethrocutaneous fistula and urethral meatal stenosis. They occur in about 10–15% of cases and are more prevalent in extensive or repeat hypospadias repair. Although less common, one may also see urethral stricture, urethral diverticulum, persistent chordee, or redundant shaft skin.<sup>84,85</sup>

Esposito et al reported on complications of pediatric urologic laparoscopy.<sup>82</sup> Over a 3-year period, 4350 laparoscopic procedures were performed at 8 Italian pediatric surgery centers: 414 cases were for cryptorchidism and 37 cases involved ambiguous genitalia. The majority of these cases were gonadectomy. Only a 2.7% complication rate, of which 6 cases required conversion to open surgery, was noted. There was no mortality in their series, with a maximum follow-up of 4 years, and only one of their complications requiring open conversion occurred during an orchiopexy.

Treatment of the child with intersex should not end with the first postoperative visit. A boy should be evaluated 1 year after orchiopexy for testes size, location, and viability. Starting at puberty, the boy should also be shown how to perform monthly testicular self-examinations. The parents should be made aware of the issues regarding cancer and infertility. Cryptorchidism places the patient at increased risks for malignant testicular tumor development (22 times the general population). Orchiopexy is not protective against testis cancer development, but it does allow easier palpation for subsequent physical examinations. Although intra-abdominal testes comprise only 10–15% of all undescended testes, they account for almost 50% of those testes which develop into cancer. The most common tumor in an undescended testes is a seminoma, which is also more common in abdominal vs inguinal testes. Up to 30% of dysgenetic testes may develop cancer, most commonly a benign tumor called gonadoblastoma. Although this tumor does not spread, it can develop into a malignant form called a dysgerminoma. Patients with a 45X/45XY mosaic karyotype also have an increased risk of carcinoma-in-situ (CIS). Some surgeons have recommended ultrasound and biopsy of a testis at puberty. Ultrasound is then performed yearly until age 20, when a repeat biopsy is performed. Absence of CIS at age 20 suggests that the risk of CIS is minimal.<sup>14,15,70</sup>

The patient with hypospadias repaired as a child should remain in follow-up with his physician in order to identify and correct any long-term complications of the surgery. It is also important to document adequate control of voiding and the force of urinary stream. There appear to be no decreases in fertility from a urethral point of view other than that previously described for cryptorchidism.

## Conclusion

Cosmetic and functional results improve yearly with advances in optical magnification, instrumentation and sutures, and tissue handling. Continuous research in this area allows

the surgeon to refine his technique and provide the patient with the best repair possible. Girls who have undergone a feminizing genitoplasty again require long-term follow-up for issues of menstruation, intercourse, and sensation as previously described. With a proper assignment of sex of rearing and a continued management with continuity of care, intersex individuals should be able to lead well-adjusted lives and ultimately obtain sexual satisfaction. Simple, yet comprehensive discussions with all physicians involved and the parents must take into account parental anxieties, and social, cultural, and religious views in order to obtain appropriate gender assignment.

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## Laparoscopy and cryptorchidism

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### Introduction

The term cryptorchidism refers to the absence of a testicle in the scrotum. During embryonic life, the testis differentiates adjacent to the mesonephric kidneys and normally descends via the inguinal canal to its scrotal position. However, in 0.8–1.8% of 1-year-old boys,<sup>1,2</sup> this process is faulty, resulting in cryptorchidism. In the majority of cryptorchid boys, a testicle is palpable in the groin, but in about 20% a testicle is nonpalpable.<sup>3</sup> In these cases, the gonad might be absent, intra-abdominal (along the normal path of descent or ectopic) or within the inguinal canal (canalicular).<sup>4,5</sup> Prior to 1976, surgical management of the nonpalpable testicle consisted of inguinal exploration with extension of the exploration into the peritoneum if the testis, nubbin, or blind-ending vessels were not identified. The testicle was either absent, removed, positioned scrotally, or a rare worst case scenario, not located by the surgeon.

In 1976, Cortesi described diagnostic laparoscopy as a method to localize the nonpalpable testicle.<sup>6</sup> Soon thereafter, therapeutic laparoscopy was performed by Bloom,<sup>7</sup> Jordan et al.,<sup>8</sup> and Bogaert et al.<sup>9</sup> With the introduction of these techniques, the management of the nonpalpable testicle has become a heated debate among pediatric urologists,<sup>10–12</sup> with camps divided for and against laparoscopic management. Nevertheless, as the years have passed, laparoscopic approaches to the nonpalpable testicle have become accepted and incorporated into daily practice by most pediatric urologists, both in the United States and abroad. In this chapter, we will review the preoperative issues, goals, timing, management decisions, procedures, and outcomes of laparoscopic management of the nonpalpable testis.

### Preoperative assessment

At initial evaluation of the patient, a history of palpable gonads, hypospadias, genital surgery or inguinal herniorrhaphy should be obtained. A careful, nonthreatening physical examination in a warm environment with warm lubricant on the groin is often crucial to identify a difficult-to-feel testicle. Note is made of the size of the contralateral testicle, if descended. If the contralateral descended testicle manifests compensatory hypertrophy (as judged by growth comparison to standard nomograms), this may indicate the lack of functioning testicular tissue on the nonpalpable side.<sup>13,14</sup> However, this finding is not absolutely accurate, and therefore the nonpalpable side must be further evaluated. Bilateral nonpalpable testicles represent a distinct subgroup that is discussed later.

Several diagnostic modalities have been used preoperatively in the evaluation of the patient with a nonpalpable testicle, including hormonal challenge and/or radiologic tests. Any diagnostic test that is utilized for the diagnosis of the nonpalpable testicle must uniformly and unequivocally determine the presence or absence of gonadal tissue, and localize it. Only laparoscopy uniformly accomplishes these goals.<sup>5,15,16</sup>

### *Hormonal challenge*

Hormonal therapy has promoted testicular descent in some nonpalpable cases, rendering some testicles palpable and even rarely fully descended.<sup>17</sup> Although rarely therapeutic, this therapy is best applied to the patient with bilateral nonpalpable testes (discussed below). The use of hormonal therapy in an attempt to promote descent, to our knowledge, in no way complicates either open orchiopexy or laparoscopic orchiopexy. The cost-effectiveness of this approach has been called into question, however.<sup>18</sup>

### *Radiological evaluation*

Many radiologic techniques, such as ultrasound, venography, computed tomography (CT), and magnetic resonance imaging (MRI), have been employed to locate the nonpalpable testis, but unfortunately all of these modalities lack sufficient sensitivity to be solely relied upon.<sup>2,19–22</sup> Herniography, venography, and arteriography may give indirect evidence, but none equivocally define the gonad. Radiographic localizing studies suffer from the inability to rule out the presence of an intra-abdominal testis;<sup>19</sup> therefore, they cannot preclude surgery in the child with a nonpalpable testicle. Granted, ultrasound does image the nonpalpable undescended testicle in some cases; however, many an inguinal orchiopexy has been undertaken when an ultrasound has shown an ‘inguinal gonad’ which turns out to be a lymph node. While MRI or gadolinium-enhanced magnetic resonance angiography (MRA) has better sensitivity,<sup>23</sup> it is still not nearly as accurate as laparoscopy has been shown to be. Any utility of MRI and MRA is completely negated due to cost issues and the requirement of an anesthetic. Surgical exploration is still required.

Radiographic imaging studies may be useful in certain clinical circumstances. Inguinal ultrasound may help identify nonpalpable inguinal and abdominal testicles in select patients who are likely to derive maximal benefit from laparoscopy,<sup>21</sup> although examination under anesthesia at the time of orchiopexy is probably equally helpful.<sup>5</sup> Imaging is also used for unusual cases, such as the overweight boy with a nonpalpable inguinal testis and the follow-up of adolescents who, because of comorbid conditions, are not surgical candidates.

### **Timing of surgery**

At birth and into the first year of life, undescended testicles have been shown to have normal histology, including a normal population of germ cells. However, beyond 18 months of age, both light and electron microscopy demonstrate histologic changes, suggesting deterioration of the germ cell population of the testis.<sup>24,25</sup> Some reports have

even noted testicular damage as early as 6 months in the human cryptorchid testis. Histology correlates with testicular position, with worse features seen in higher testicles. On the other hand, spontaneous testicular descent has been noted postnatally as late as 4–6 months of age. Therefore, the current recommendation concerning timing of orchiopexy would be between ages 6 and 12 months, since the risks of anesthesia in a healthy 6-month-old child are similar to that of a healthy adult. In addition, there may be anatomic and technical advantages to orchiopexy within the first 6 months, especially in patients with high undescended testicles with prune-belly syndrome. This approach maximizes the opportunity for those few testicles that will descend during the first year of life, while preventing the histologic changes that occur in those testicles that remain maldescended beyond the first year of life. Data supporting this 'early orchiopexy' recommendation are being reported; testicular growth is more common in children operated prior to 18 months than when older,<sup>26</sup> and early orchiopexy seems to benefit adulthood Leydig cell function, thereby potentially enhancing fertility.<sup>27</sup>

Decisions regarding orchiopexy after age 2 years old are based on the risks/benefits of the testicle to the individual. Although an undescended testis may function poorly for fertility, the usefulness in terms of androgen production must be considered, especially in cases of a solitary testicle.

Occasionally, a postpubertal male is found to have an undescended testis, palpable or nonpalpable. Rarely are sperm noted in these testes<sup>28</sup> and these testes are at significant risk for malignant change. An updated analysis of the anesthetic risks of orchiectomy vs the lifetime risk of germ cell cancer was performed by Kibel and colleagues.<sup>29</sup> They advocate orchiectomy in all healthy, cryptorchid males until age 50 years. For some patients with comorbid conditions, the risks of surgery may be significant even before this age is reached. If not palpable, diagnostic laparoscopy with laparoscopic orchiectomy (especially if combined with another surgical procedure) is an optimal means of management that minimizes pain and time away from work, and scarring.

## **Laparoscopic management of the nonpalpable testis**

### *Definitions, goals, and indications*

Laparoscopy has been found to be useful for both the diagnosis of the unilateral or bilateral nonpalpable testicle (diagnostic laparoscopy) as well as for the management of the nonpalpable testicle (therapeutic laparoscopy). Laparoscopy is an excellent diagnostic approach to verify the existence and to locate the nonpalpable testicle.<sup>30–33</sup> The principal goal of diagnostic laparoscopy is to determine if there is nonpalpable testicular tissue. If there is nonpalpable testicular tissue, then the decision must be made as to whether the testicle is suitable for orchiopexy or better removed. In addition, mobility of the testis, its vas deferens, and its vascular supply is assessed, a crucial feature in planning the therapeutic surgical approach. The goal of therapeutic laparoscopy for the undescended testicle is either removal of the poor testicle or permanent fixation of the testicle in the scrotum. Therapeutic laparoscopy thus encompasses the options of laparoscopic orchiectomy, primary laparoscopic orchiopexy, laparoscopic one-stage Fowler-Stephens orchiopexy, or laparoscopic two-stage Fowler-Stephens orchiopexy. The

indications/goals of laparoscopic orchiopexy are identical to the goals of open orchiopexy: namely, to improve fertility (and possibly diminish malignant transformation potential), relocate the testicle to the scrotum for easier examination, correct the associated inguinal hernia, prevent testicular torsion, and alleviate possible psychological trauma resulting from an empty hemiscrotum.<sup>34</sup>

### *Alternative therapy*

Management of the nonpalpable testis can be medical (hormonal therapy as previously described) or surgical. Surgical options include open techniques (inguinal exploration with the extension of the inguinal incision proximally to explore the abdomen or primary open abdominal approach), or laparoscopic techniques. Both techniques offer significant advantages and disadvantages.

### *Disadvantages to open inguinal exploration*

Serious concerns exist in the reliability of an open inguinal exploration to rule out an intra-abdominal testis. Pooling data from five series,<sup>32,35–39</sup> laparoscopy has identified 42 testicles in 86 ‘negative’ open explorations for a nonpalpable testicle. Although a large sampling bias is expected in such reports, the fact that testicles are missed by open inguinal exploration but found by laparoscopy cannot be ignored, considering intra-abdominal testes are at highest risk for malignant degeneration.

Moreover, a critical assessment of the surgical outcomes of open orchiopexy for the intra-abdominal testicle reveals the need for improvement.<sup>40,41</sup> At present, therapeutic laparoscopy offers the highest success rate for orchiopexy for the intra-abdominal testicle.<sup>38</sup>

### *Disadvantages to diagnostic and therapeutic laparoscopy*

Opponents of therapeutic laparoscopic orchiopexy have voiced concerns about the long incision in the peritoneum, lengthy operation, higher operating room costs, potential injury to intra-abdominal or retroperitoneal organs, and the long-term risk of adhesions.<sup>42</sup> Operating room costs can be diminished by the use of reusable equipment<sup>43</sup> and countered by shorter and simpler hospitalization.<sup>44</sup> The incidence of adhesion formation from pediatric urologic laparoscopic procedures is lower than that expected with open exploration.<sup>45,46</sup> Clearly, as with any surgical approach, laparoscopy may have complications.<sup>38</sup> In addition, opponents argue that a laparoscopic approach subjects a patient (with an inguinal testis or nubbin) to an unnecessary laparoscopic procedure in 37–64% of cases.<sup>10,11,15,47</sup> This can be reduced significantly by first performing scrotal exploration when there is any palpable tissue. The finding of hemosiderin or a nubbin with vas and atretic vessels obviates the need for further exploration.<sup>48</sup>

### *Advantages to diagnostic and therapeutic laparoscopy*

Against this view, advocates of laparoscopy for the nonpalpable testis have noted that it is useful in at least 43–51% of unilateral cases to identify either absence (27%) or an

intra-abdominal testicle (16–21%), and for bilateral undescended testicle in 75% of cases, with 17% blind-ending vessels and 58% intra-abdominal testicles,<sup>49</sup> although these numbers vary from study to study. Thereby, an unnecessary inguinal exploration with subsequent extended open abdominal exploration can be avoided in the Vanishing testis' syndrome and testicular aplasia. Other reports site intra-abdominal viable testicles as high as 52%.<sup>5,50</sup> Thus, surgical planning is improved. Several rare conditions, including absent vasa and vessels with a retroperitoneal testis,<sup>15</sup> persistent müllerian ducts,<sup>51</sup> other intersex states,<sup>52</sup> transverse testicular ectopia, polyorchidism, and gonadal dysjunction from the wolffian ducts, can best be identified and treated simultaneously laparoscopically. Careful intra-abdominal mobilization can be extensive with therapeutic laparoscopy, allowing orchiopexy with or without testicular vessel division. In addition, laparoscopic orchiopexy offers less trauma of access, a rapid recovery, minimal adhesion formation,<sup>45</sup> and potentially less psychological burden from surgery and scarring. In skillful hands, the operating time for laparoscopic orchiopexy becomes equivalent to open abdominal orchiopexy. A time of less than 90 min for bilateral orchiopexy for abdominal testicles is reasonable to expect in most cases.

## **Laparoscopic surgery**

### *Unilateral nonpalpable testes*

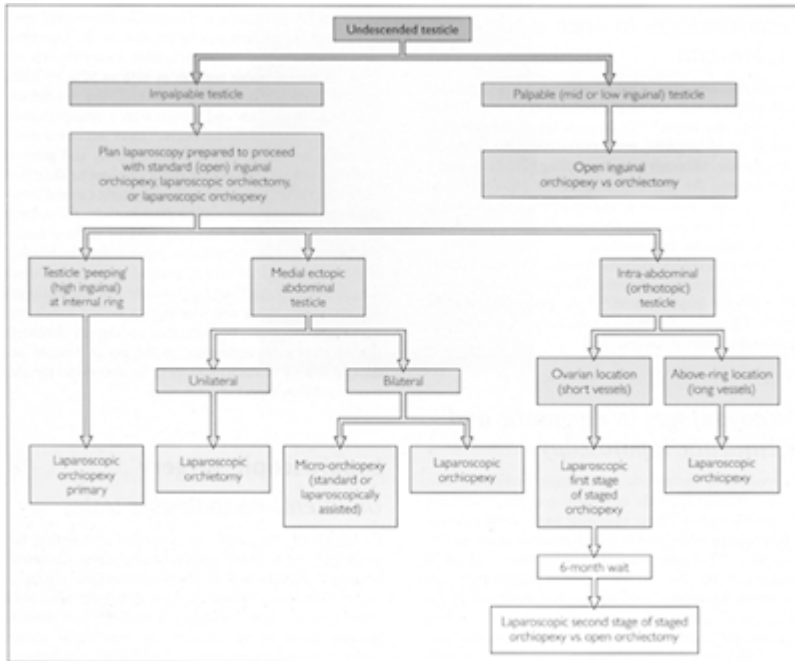
Preoperatively, the family is counseled concerning the possibilities of an absent testicle, small atrophic testicle, or an intra-abdominal testicle. The possible surgical scenarios are then presented. If a testicle is palpable under anesthesia (18%),<sup>5</sup> an inguinal orchiopexy is performed. If there is palpable tissue in the scrotum, an expeditious scrotal exploration may be performed, looking for a nubbin or deposit of hemosiderin, vas and atretic vessels, all suggesting no need for further exploration.<sup>48</sup> If it remains nonpalpable under anesthesia, then diagnostic laparoscopy is performed. If an atrophic testicular remnant is identified, a laparoscopic orchiectomy might be performed (surgeon's bias). If a subjectively good testicle is found, the laparoscopic options include (1) primary laparoscopic orchiopexy, (2) one-stage Fowler-Stephens orchiopexy, or (3) two-stage Fowler-Stephens orchiopexy (second stage follows 6 months later). The risks of surgery include bleeding, infection, anesthesia risks, injury to intra-abdominal or retroperitoneal organs necessitating emergent laparotomy, loss of a testicle (acute atrophy), mechanical injury to the vas, epididymis, testicular vessels or testis, poor testicular position, or need for a two-stage procedure. An algorithm illustrating the approach to management of the nonpalpable undescended testicle is shown in Figure 63.1.

### *Techniques of procedures*

#### **Diagnostic laparoscopy**

After adequate anesthesia is attained, the patient is secured to the bed in the supine, frog-leg position with arms tucked. Preparation and draping must be suitable for an open abdominal procedure, be it planned or necessary. A urethral Foley catheter and an

orogastric tube are passed. All laparoscopic equipment is assembled and verified. A supra- or infraumbilical skin incision is made and peritoneal access is obtained. Several techniques have been used, including Veress needle, Hasson access, or open access. Given most patients are between 6 and 24 months of age, safety concerns have led most surgeons to abandon blind access techniques (Veress needle) and to use open



**Figure 63.1**

Algorithm for management of the undescended testicle.

access techniques. Holding sutures are placed in the fascia to help elevate it for the peritonotomy. The authors use the InnerDyne Step introducer system,<sup>53,54</sup> a radially dilating access sheath, to achieve 5 or 10 mm access.<sup>55</sup> Alternatively, exclusively needlescopic 2 mm access (and working ports) can be used, as reported by Gill and colleagues,<sup>53,56,57</sup> but they provide less light and a smaller visual field. After insufflation to 14 cmH<sub>2</sub>O, a 5 mm 0° camera is used to inspect the abdomen for injury. The patient is then placed in the Trendelenburg position and each internal ring is inspected bilaterally. On the unaffected side, the testicular vessels and vas are easily identified, leaving the closed internal ring (Figure 63.2). Caudal traction on the descended testis can help visualization of its cord structures. On the affected side, the internal ring is noted and the testicle, vas, and testicular vessels are sought. Several findings are possible on the affected side:

1. If the ring is closed with a normal vas and normal testicular vessels exiting (see Figure 63.2), the groin is explored for the testis or nubbin by a laparoscopic or open approach. The removal of any remaining testicular nubbin is controversial since 10% of nubbins may contain viable germ cells<sup>58-60</sup> and theoretically could undergo malignant change.
2. If normal-appearing vas and testicular vessels exit an open internal ring (Figure 63.3), the inguinal canal can be 'milked' retrograde in an attempt to push a canalicular (peeping) testicle or nubbin into the abdomen (Figure 63.4). In any case, if the gonad is not found, the groin must be explored,<sup>61</sup> either by open or laparoscopic techniques.



**Figure 63.2**

The laparoscopic appearance of a normal left groin. The spermatic vessel leash can be seen joined by the vas deferens passing through a closed internal ring. Traction is on the testicle, emphasizing the location of the ring.

3. If blind-ending vessels are clearly identified, ending in a 'horse tail' appearance and often within proximity to a blind-ending vas, the testis is not viable and the procedure is terminated, although some surgeons again would remove any testicular nubbin found (Figure 63.5).
4. An intra-abdominal testis could be found (Figure 63.6).
5. A blind-ending vas can be seen without testicular vessels in the vicinity. In this case, the laparoscopic exploration is not complete and must continue rostrally toward the aortic origin of the testicular vessels until the gonad is found. This finding is termed gonadal dysjunction.

Statistically, in nonpalpable cases, an intra-abdominal testis or peeping testicle is identified in 50–60%, an atrophic nubbin in 30%, and an absent testis in 20%. If a testicle is found, it can be seen within 2 cm of the internal ring (30.6%) or peeping (17.4%), typically of normal size with a normal-appearing epididymis, vas, and vessels.

Alternatively, the testicle can be found  $>2$  cm from the internal ring, either along the normal path of descent (44.8%) or in such ectopic sites as beside the bladder, rectum, kidney, liver, spleen, or crossed ectopia (7.1%).<sup>38</sup>

In some cases, the testicle and testicular vessels are not clearly identified with the camera alone. A manipulating instrument is useful to visualize the testicular vessels (if loops of bowel are blocking the view). The Veress needle or other small probes have been used for this purpose and do not require a formal secondary cannula placement. If therapeutic laparoscopy is indicated, the insufflation is



**Figure 63.3**

The laparoscopic appearance of the right groin in which there is a patent processus vaginalis (hernia).

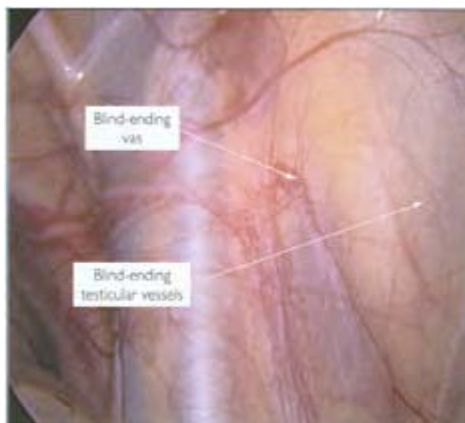


**Figure 63.4**

(A) Laparoscopic appearance of the right groin; the spermatic vessel leash joined by the vas can be seen passing



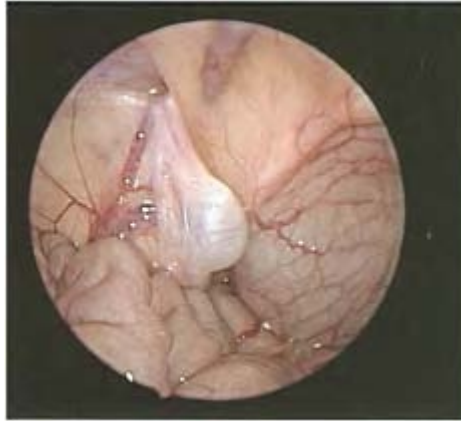
adjacent to the open internal ring (patent processus vaginalis). (B) With gentle pressure on the groin, the testicle can be seen delivered into the abdomen.



**Figure 63.5**

The laparoscopic appearance of the right groin, with the classic blind-ending vas and blind-ending testicular vessels in proximity to each other.

temporarily increased up to 20 cmH<sub>2</sub>O while two 2 mm or 5 mm ports are secured at the level of the umbilicus just lateral to the inferior epigastric vessels (Figure 63.7). Using a Maryland grasper and laparoscopic scissors with cautery, the testis is located. Either laparoscopic orchiectomy, single-stage laparoscopic orchiopexy (primary or one-stage Fowler-Stephens), or two-stage laparoscopic orchiopexy is chosen.



**Figure 63.6**

The laparoscopic appearance of the low left abdominal testicle.

**Primary laparoscopic orchiopexy**

To perform a primary laparoscopic orchiopexy, the patient is placed in the Trendelenburg position with the ipsilateral side of the bed tilted upward. A peritoneotomy is made just lateral to the testicular vessels. It is carried over the top of the internal ring and continued lateral and superior to the vas, with care to not injure the inferior epigastric vessels or



**Figure 63.7**

Typical cannula placement for left laparoscopic orchiopexy.

the bladder. While some urologists make a mirror peritoneotomy medial to the vessels and vas, others (including the authors) intentionally leave the peritoneal triangle between the testicular vessels and the vas undisturbed. Once the peritoneotomy is completed, the testicular vessels, testicle, and vas are elevated on this peritoneal pedicle, thereby dissecting the plane between these structures and the external iliac vessels (Figure 63.8). Care is taken to not harm the external iliac vessels, inferior epigastric vessels, or a long looping vas. The testicle is then retracted rostrally, inverting the processus vaginalis and the gubernaculum. The gubernaculum is thinned and cut across with electrocautery, taking care to watch for a long looping vas. Cautery is used since the gubernacular attachments are vascular, although caution is exercised to avoid thermal damage to

peritesticular structures. The testicle is then retracted toward the contralateral internal ring to assess length. In most cases, if the testicle can reach the contralateral internal ring, length is sufficient to place the testicle well in the respective hemiscrotum. While vigorous mobilization of the vas should be avoided for fear of testicular atrophy, the vas must be sufficiently mobilized to prevent ureteral kinking from the paravasal attachments. Any remaining attachments preventing testicular mobility are carefully dissected, and, once adequate length is assured, the testicle can be transferred to the scrotum.

In some instances, length is inadequate. One option is to incise the peritoneum parallel to the testicular vessels as far



**Figure 63.8**

The peritoneotomies have been completed and the gubernaculum was transected. The testis is retracted medially and ventrally, with the sheet of peritoneum medial to the testicular vessels and vas intact. Tethering attachments on the dorsal side of the peritoneum can be divided as the testis is pulled toward the contralateral internal ring.

proximal as is safe. Then, the peritoneal incision is extended perpendicular over the testicular vessels without their injury. Often this perpendicular incision significantly ‘relaxes’ the vessels, allowing scrotal positioning. If length still remains an issue and the peritoneum medial to the vas and vessels is intact, the spermatic vessels can be divided (Fowler-Stephens approach—see below).

Several techniques are described to deliver the testis into the scrotum, including retrograde placement of a clamp or port. By placing a port, the pneumoperitoneum can be maintained in the event the testis is 'fumbled'. The authors use the InnerDyne Step 5 or 10 mm for the transfer.<sup>53,54</sup> A 2 mm grasper in the ipsilateral abdominal port is passed medial or lateral to the inferior epigastric vessels, depending on length needs, just over the pubic ramus (Figure 63.9A). A scrotal skin incision is made in the ipsilateral hemiscrotum and a subdartos pouch is generated. The 2 mm grasper is passed through the scrotal incision. The Step introducer sheath is introduced retrograde over the 2 mm grasper (Figure 63.9B). The 5 or 10 mm trocar is introduced through the Step introducer (Figure 63.9C). A locking grasper is introduced through the scrotal port, the gubernaculum of the testis is grasped, and the testis is delivered via the port into the scrotum (Figure 63.10A). The testis is secured intrascrotally in the subdartos pouch by the fixation technique preferred by the surgeon (Figure 63.10B). The intra-abdominal pressure is lowered to 4 mmHg and the surgical field assessed for bleeding (Figure 63.10C).

In children, the fascia of any 5 or 10 mm port site is closed, as hernias have been reported. All CO<sub>2</sub> is evacuated and skin wounds are closed and dressed. These children do profit from adjuvant caudal anesthesia and local injection of cannula sites using bupivacaine (Marcaine). The children are awakened, recover from anesthesia, and are discharged. In most cases, the diet is rapidly advanced. With the exception of instructions to keep the child from playing on straddle implements, virtually no physical restrictions are imposed.

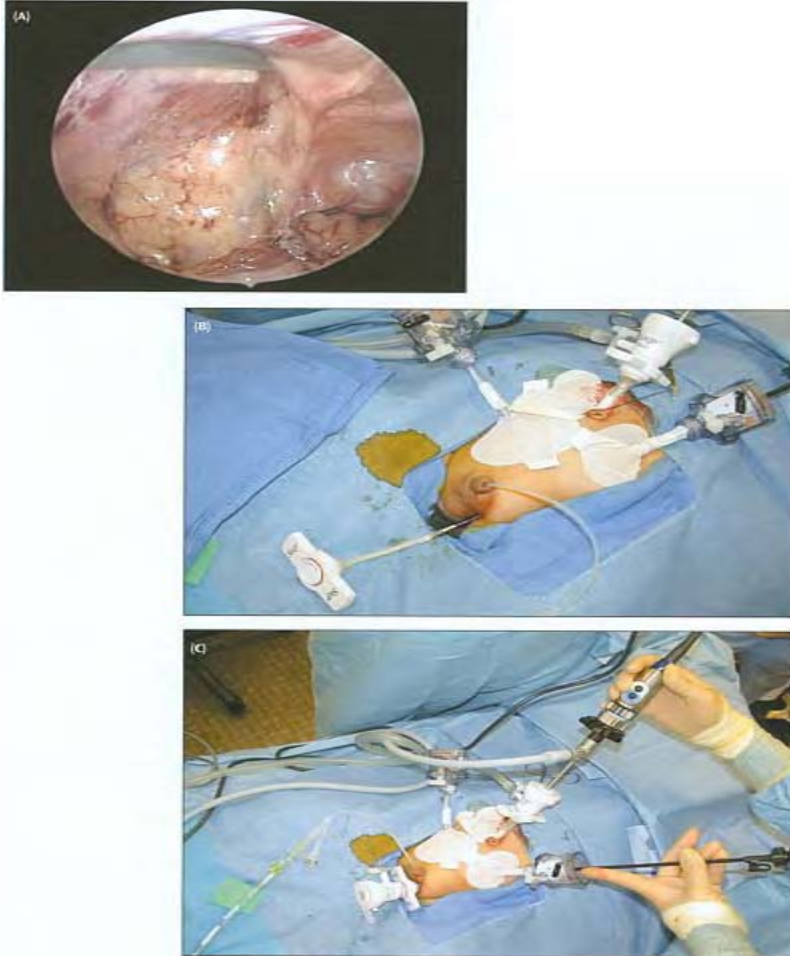
### **One-stage Fowler-Stephens laparoscopic orchiopexy**

If the maneuvers outlined above result in inadequate length of the testicular vessels preventing scrotal positioning, a one-stage Fowler-Stephens procedure can be performed. Via a contralateral 5 mm port, the testicular artery and vein are clipped and transected, preserving the vasal blood supply to the testicle and thus allowing the testicle to be placed in the scrotum with one laparoscopic procedure. However, this technique has a higher risk of testicular atrophy.<sup>38</sup>

### **Two-stage Fowler-Stephens laparoscopic orchiopexy**

If, at the time of diagnostic laparoscopy, a high testis is found which stands little chance of reaching the scrotum without transaction of the testicular vessels, a two-stage Fowler-Stephens laparoscopic orchiopexy may be used.<sup>7</sup> In this case, a contralateral 5 mm port is placed and the only peritoneotomy performed is parallel and immediately medial to the testicular vessels, a safe distance proximal to the iliac vessels. Via this peritoneotomy, the vessels are encircled and a 5 mm vascular clip applicator is used to ligate the vessels. The vessels may be transected or left in continuity after clipping, and the procedure is terminated. Six months later, a second laparoscopy is performed following the steps outlined in the primary laparoscopic orchiopexy. The vessels are mobilized to the clips and the mobilized testis is transferred into the scrotum. During the 6-month interval, collateral blood supply via the paravasal arteries is ostensibly enhanced.

Division of the spermatic vessels to 'aid' with orchiopexy was advocated as early as 1903 by Bevan.<sup>62</sup> The staged approach based on collateralization along the long loop of the vas deferens was an extension of the technique described by Fowler and Stephens. Originally a long looping vas was felt to be a prerequisite for the Fowler-Stephens procedure; however, intra-abdominal testicles with non-long looping vas deferens have been successfully addressed. The staged approach has been likened to other forms of delay, a term in the



**Figure 63.9**

(A) Via the ipsilateral abdominal port, a laparoscopic Maryland grasper is passed medial to the ipsilateral inferior epigastric vessels, over the anterior

pubic ramus, and out through the scrotal skin incision. (B) The 10 mm Step introducer is loaded on the Maryland grasper and pushed intraperitoneally as the Maryland grasper is drawn back into the abdomen. Note the Maryland grasper in the ipsilateral port exiting the scrotum. (C) The trocar is advanced into the introducer with visualization via the intra-abdominal camera.



**Figure 63.10**

(A) Photograph showing an intra-abdominal testicle being pulled into the 10 mm laparoscopic cannula using testicular grasping forceps, the testicle is then delivered to the right hemiscrotum. (B) Photograph

illustrating the outside appearance with the testicle delivered to the level of the scrotum. (C) Intra-abdominal view after the left testicle has been transferred to the scrotum.

reconstructive literature which implies the transposition of tissue at a first stage, with division of the axial blood supply at a second stage, thus allowing the transfer tissue to survive on random collateralization occurring between the first and second stage. Clearly, the staged orchiopexy does not accomplish this. Instead, the axial blood supply, or at least part of it, is divided at the first stage. There remains a second axial blood supply, but one is led to believe that the second blood supply enhances during the period between first stage and second stage. Whether this enhancement truly occurs has recently been called into question by Koff and Sefhic.<sup>63</sup> Clinically, most would agree that the paravasal blood supply, after division of the spermatic vessel leash and a waiting period, does appear to be more prominent. After a 6-month wait following the initial ligation of the spermatic vessels, using either laparoscopic techniques or an open technique, the testicle is brought to the scrotum based on the paravasal vascular supply.

### Intraoperative scenarios

**Common scenarios.** If normal vessels enter an open or closed ring, an inguinal exploration can be accomplished laparoscopically in virtually all cases. In the case of a high canalicular testis (peeping testis), laparoscopic orchiopexy has been shown to be effective. In the vast majority of low abdominal testes (<2 cm from the internal ring), primary laparoscopic orchiopexy is most effective. For testes >2 cm from the internal ring, many would consider staged orchiopexy.

**The blind-ending vas and the medially ectopic testis.** It cannot be overemphasized that the undescended testicle is found proximate to the vessels, not necessarily the blind-ending vas. If one finds only a blind-ending vas deferens in the pelvis, one cannot declare the testicle 'vanished' without further exploration and the findings of blind-ending vessels. Occasionally, the gubernacula can appear vascular enough to represent testicular vessels, and give the mistaken impression of vas and vessels exiting the ring when a testis exists proximally.

During descent, the medial ectopic abdominal testicle comes to rest medial to its respective medial umbilical artery. Associated with these testicles are readily apparent vascular gubernacular structures that extend to the respective location of a normal internal ring, usually closed (i.e. no patent processus vaginalis). The vas deferens is quite short; most of these testicles have not been noted to have looping vas or disassociation of the paratesticular tubular structures, and, by definition, the spermatic vessel leash is short. Although these testicles can occasionally be placed in the scrotum using laparoscopic techniques, this is often technically difficult. Also because these testicles are already medial to the obliterated umbilical artery, the advantages of medial transposition are negated. Because the testicles are not associated with looping of the vas, the advantages of spermatic vessel division, either primary or staged, are likewise negated. These



testicles appear to be quite 'ovarian'. The prominent gubernacular vessels are very similar to a round ligament in appearance. There is often a very prominent peritoneal fold, reminiscent of the broad ligament. The testicles, as opposed to having a vertical orientation, appear to have a horizontal orientation. If unilateral, consider orchiectomy or staged laparoscopic orchiopexy. If associated with bilateral maldescensus, aggressive mobilization can be attempted. Another option in the case of bilaterality would be the microvascular reanastomosis of the free transferred testicles.

### *Bilateral nonpalpable testes*

At birth, approximately 1/600 males have bilateral undescended testes, representing 10–25% of patients with cryptorchidism. Given that normally testicular descent is an event of the third trimester, this may be a common physical finding in premature male neonates. It is estimated that at least 6% of patients with bilateral undescended testes have an endocrine disorder as the etiology.<sup>64,65</sup>

Bilateral undescended testes, when each is palpable, are managed in the same fashion as unilateral palpable undescended testes. However, the finding of bilateral nonpalpable testes represents a special situation that may have life-threatening implications in the neonatal period, especially in association with severe hypospadias. The differential diagnosis of bilateral nonpalpable cryptorchidism includes anorchidism, undescended testicles (bilateral or unilateral with contralateral absence), and ambiguous genitalia due to female pseudohermaphroditism or another intersex condition. It is this last possibility that necessitates an urgent and thorough evaluation to rule out life-threatening congenital adrenal hyperplasia (CAH). A karyotype, endocrine testing, radiographic studies and, if indicated, laparoscopy usually provide the necessary information to make an intersex diagnosis. A normal-appearing masculinized phallus does not eliminate this possibility. Routine neonatal screening for CAH has aided detection of this entity.

In the case where an intersex disorder has been excluded, endocrine studies—human chorionic gonadotropin (hCG) stimulation test, serum müllerian inhibitory substance (MIS) level, or serum inhibin B level—may be useful to differentiate bilateral cryptorchidism from anorchia.<sup>66</sup> hCG administration can be used to stimulate testosterone production by testicular tissue to detect its presence biochemically, and may also cause the gonads to become palpable by physical examination. However, false-negative hCG stimulation testing can occur due to an unresponsive population of Leydig cells. In addition, no consensus has been reached concerning dosing and frequency of hCG. Therefore, hCG stimulation testing is combined with the measurement of gonadotropins to diagnose anorchia. Markedly elevated gonadotropins before puberty are indicative of anorchidism,<sup>66</sup> but all boys with normal serum gonadotropin levels must undergo exploration regardless of the outcome of the hCG stimulation test. Measurement of serum MIS can be used to provide additional evidence that testicular tissue is present and has recently become widely available. Recently, in prepubertal cryptorchid children, the serum inhibin B level has been shown to negatively correlate with serum follicle-stimulating hormone (FSH) levels (basal or hCG stimulated)<sup>67</sup> and positively correlate with the lack of testosterone response to hCG stimulation.<sup>68</sup> However, serum inhibin B levels can also be somewhat low in children with gonadal dysgenesis or the history of

testicular trauma. If the clinical experience with this new available serum marker continues to show its reliability, this may supplant the need for the hCG stimulation test.

Thus, with a male genotype, the diagnosis of anorchia can be made with a low serum testosterone, a negative hCG stimulation test, increased serum gonadotropins, a negative serum MIS, a low basal serum inhibin B level, normal levels of adrenal steroid precursors, and radiographic studies demonstrating the absence of müllerian structures. In equivocal cases, diagnostic laparoscopy and/or open surgical exploration with gonadal biopsy may be required to confirm the diagnosis of anorchia. However, some pediatric urologists feel that for the child with bilateral nonpalpable testicles, laparoscopic management is imperative, regardless of the laboratory results after hCG stimulation or serum MIS sampling.

Intraoperative decision making is impacted by the location of the testes with bilateral disease. In patients with high bilateral intra-abdominal testes, most pediatric urologists perform staged reconstructions. Surgery is completed on one side, confirming unilateral testis survival prior to embarking on the contralateral side, since in many of these complex cases a Fowler-Stephens approach must be used.

### **Laparoscopic orchiopexy for intersex states**

Diagnostic laparoscopy was first described for intersex evaluation in 1973 by Gans and Berci.<sup>69</sup> Advancements in the laboratory diagnosis of intersex states mean the majority of cases have a clear-cut diagnosis prior to surgery. Exceptions include differentiating between true hermaphroditism and the XX male with genital ambiguity and nonpalpable gonads.<sup>52</sup> Nevertheless, therapeutic laparoscopic techniques including laparoscopic gonadal biopsy, gonadectomy (for dysgenetic gonads or when contrary to sex assignment), orchiopexy, and in some cases removal of ductal structures, have a prominent place in the management of intersex children (primarily male pseudohermaphrodites). Minimalization of physical scarring from surgery is paramount in this patient population, who often suffer from poor body and sexual self-esteem.

### **Benefits of surgery**

By performing an orchiopexy, the often-associated inguinal hernia is repaired and the testicle is fixated in the scrotum, thereby preventing torsion and any psychological issues associated with an empty hemiscrotum.

### **Fertility**

Clinically, decreased fertility is a well-recognized consequence of cryptorchidism. Even after orchiopexy, fertility is impaired in approximately 50–70% of boys born with one undescended testis and up to 75% of those born with two undescended testes.<sup>70</sup> Since histologic deterioration is thought to be worse with higher testes, fertility has been thought to vary in association with this finding. However, a recent study indicates that

paternity (which does not necessarily correlate with histology of the undescended testis in cases of unilateral maldescent) may be similar in both abdominal and extra-abdominal unilateral undescended testes.<sup>71</sup> Since the serum level of inhibin B is considered to reflect Sertoli cell function and seminiferous tubule integrity, the finding of lower levels of circulating inhibin B in boys with a history of cryptorchidism may predict impaired spermatogenesis later in life.<sup>72</sup> Whether or not early orchiopey ultimately improves fertility remains to be seen. Without treatment, bilateral cryptorchidism ultimately results in infertility. Antisperm antibodies, abnormalities of the epididymis and vas deferens, and surgical injury to the vas deferens during orchiopey may also contribute to infertility in patients with a history of cryptorchidism.

### **Testicular malignancy**

Despite the increased risk (9.7×) over the general population, the likelihood of developing testicular cancer in a man with a history of cryptorchidism is no more than 1 in 2000. For this reason, removal of undescended testes is not warranted in the general case. Orchiopey allows easy examination of the scrotal testis for earlier detection in cases of testicular cancer. Unfortunately, there is no strong evidence that early orchiopey decreases the risk of testicular cancer.<sup>73</sup>

### **Complications of diagnostic and therapeutic laparoscopy for the nonpalpable testis**

Diagnostic laparoscopy is regarded as a highly effective and safe procedure to localize and diagnose the nature of the nonpalpable testicle. In most series, a large number of procedures have been performed with >95% accuracy.<sup>5</sup> Many of the complications of laparoscopic orchiopey have been associated with blind cannula placement Veress needle insufflation, which is discouraged by the authors. Major complications that have been reported with laparoscopic orchiopey include acute testicular atrophy, bowel perforation,<sup>74</sup> cecal volvulus, bladder perforation,<sup>9</sup> ileus, minor vas laceration, bowel incarceration at the site of the closure of the parietal peritoneum, and spermatic vessel avulsion, which leads to a one-stage Fowler-Stephens orchiopey.<sup>38</sup>

### **Outcomes of laparoscopic orchiopey**

Outcomes analyses always compare to a gold standard. In the case of orchiopey, open surgical techniques are the gold standard, with the early postoperative outcome variables being testis position (scrotal) and lack of testicular atrophy. In 1995, a meta-analysis of open surgical results<sup>40</sup> found open orchiopey for the intra-abdominal testicle to yield an overall 76.1% success rate. By procedure, open one-stage Fowler-Stephens orchiopey yielded a 67% success rate, whereas the two-stage procedure yielded 73%. Transabdominal orchiopey was successful in 81%, whereas micro vascular orchiopey worked in 84%. In comparison, a 2001 multi-institutional analysis of laparoscopic

orchiopexy was performed, collating the results from 10 US centers.<sup>38</sup> A total of 310 laparoscopic orchiopexies in 252 patients in a 9-year period were included; 15.2% were lost to follow-up. Primary laparoscopic orchiopexy was successful in 97.2% of 178 testes. One-stage Fowler-Stephens laparoscopic orchiopexy was successful in 74.1% of 27 testes, whereas two-stage Fowler-Stephens laparoscopic orchiopexy was successful in 87.9% of 58 testes. Therefore, if the Docimo 1995 meta-analysis is compared for each type of orchiopexy, the laparoscopic approach yielded higher success rates than the same approach performed open (Table 63.1). In addition, both analyses revealed that one-stage Fowler-Stephens approaches had a significantly higher atrophy rate than the two-stage repair.

In summary, laparoscopic orchiopexy has been found effective, in one modification or another, for the management of all testicles from high canalicular, associated with hernias, to high abdominal. However, the higher the testicle, the more profound the anatomic aberrances. The long-term function of these testes with respect to malignant degenerative potential and fertility will be outcomes analyzed by the next generation of pediatric urologists. The issue then surrounds the advocacy of performing orchiopexy for the severely dysmorphic abdominal testicle. That issue has been extensively argued and will continue to be. However, the development of sperm aspiration techniques associated with various applications of assisted fertilization seems to favor a try at orchiopexy as opposed to reflexive orchiectomy.

## Conclusions

Laparoscopy for the nonpalpable testis has become the standard approach at many US and European centers. Although laparoscopy is invasive and requires general anesthesia, the advantages are felt by most to far outweigh the disadvantages, particularly now that the laparoscopy can be part of the management, as opposed to just the preparation. The experienced surgeon can accomplish identical or even improved surgical results with similar

**Table 63.1** *A comparison of open vs laparoscopic orchiopexy success rates from two large published series. Success was defined as scrotal position and lack of atrophy*

| Study                                 | Primary orchiopexy |         | One stage F-S |         | Two stage F-S |         |
|---------------------------------------|--------------------|---------|---------------|---------|---------------|---------|
|                                       | <i>n</i>           | Percent | <i>n</i>      | Percent | <i>n</i>      | Percent |
| Open orchiopexy <sup>40</sup>         | 80                 | 81.3    | 321           | 66.7    | 56            | 76.8    |
| Laparoscopic orchiopexy <sup>38</sup> | 178                | 97.2    | 27            | 74.1    | 58            | 87.9    |

*n*=number of testes, F-S=Fowler-Stephens.

operative time and diminished surgical morbidity using laparoscopic techniques. It is clear that laparoscopic orchiopexy provides higher retroperitoneal mobilization of the testicular vessels and vas than can be achieved via inguinal open approaches. Given several reports<sup>32,35-39</sup> of testes found laparoscopically after false-negative inguinal

explorations, the reports of carcinoma-in-situ in postpubertal cryptorchid patients,<sup>28,75</sup> and numerous cases of malignancy in retained intra-abdominal testes,<sup>76</sup> a consistent definitive diagnosis by laparoscopy is imperative and outweighs the price of its invasiveness. Laparoscopic orchiopexy is, if not the procedure of choice, an acceptable and successful approach to the nonpalpable testis. Sometimes called a technology seeking an application,<sup>77</sup> it is currently the procedure associated with the highest testicular success rate (scrotal position without testicular atrophy).<sup>38</sup>

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## Minimally invasive management of pediatric urinary calculus disease

Michael J Erhard

### **Etiology/Epidemiology**

Urinary stone disease in children is relatively rare in developed countries although it is recently observed to be increasing in frequency.<sup>1</sup> Significant renal calculus disease remains endemic in many developing nations, most likely due to dietary and infectious etiologies. In the United States the most common presenting symptoms include abdominal pain (40–75%), gross or microscopic hematuria (25–40%), and symptoms attributable to urinary tract infections (10–30%).<sup>2–6</sup>

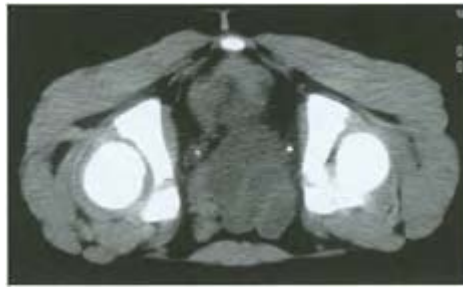
Spontaneous passage of a calculus is possible; therefore, conservative management should be undertaken unless there is obstructive uropathy, urosepsis or uncontrolled pain and vomiting. The rate of spontaneous passage will vary according to both the size of the stone and position within the ureter. Adult studies show an overall spontaneous passage of approximately 55% for all stones with those less than 4 mm passing approximately 80% of the time.<sup>7</sup> Other studies have shown that stones within the proximal collecting system pass approximately 22% of the time compared with 46% and 71% for those in the middle and distal third of the ureter.<sup>8</sup> Previous reports in the pediatric literature concluded that calculi less than 3 mm have a greater chance of passing spontaneously while stones larger than 4 mm most likely require surgical management.<sup>9</sup> It has been this author's experience that even small stones which become symptomatic in the proximal ureter are often not likely to advance spontaneously (Figure 64.1). All recommendations are meant to be general guidelines, and every situation needs to be managed individually.

If the clinical symptomatology suggests the presence of a urinary calculus, the most appropriate radiographic evaluation is a nonenhanced helical computed tomography (CT) scan of the abdomen and pelvis<sup>10,11</sup> (Figure 64.2). This will allow complete visualization of the collecting system and we will be able to identify all sizes and types of



**Figure 64.1**

Even large stones with smooth edges and a tapered leading edge, may pass through the pediatric ureter, therefore conservative management should be the first step unless symptoms warrant urgent intervention.



**Figure 64.2**

This young boy had right-sided symptoms and was found on nonenhanced CT scan of the pelvis to have bilateral ureteral calculi.

urinary calculi. If deemed necessary, intravenous contrast media can be administered after the noncontrast phase to evaluate for obstruction and focal changes in the kidney, providing more information than a traditional



**Figure 64.3**

Many stones can be visualized on plain x-ray of the abdomen, but this should not be a first line x-ray in the evaluation of the symptomatic child due to lack of sensitivity. Also, no anatomic information of the collecting system is obtained making this a less than ideal study.

intravenous pyelogram (IVP). Most pediatric stones are radiopaque and consist of calcium oxalate, which may enable them to be visualized on plain x-ray (Figure 64.3). Although ultrasound is usually still performed to exclude large renal calculi, hydronephrosis or perirenal collections, it has very low sensitivity for detecting ureteral calculi.<sup>12</sup> Total radiation exposure in children is a serious consideration, and CT protocols with minimum dosage need to be devised.<sup>11,13</sup>

Metabolic and genitourinary anomalies which predispose to urolithiasis often coexist in pediatric patients. Metabolic abnormalities have been reported in approximately 48–86% of children with urinary stones.<sup>5,14–16</sup> Common urine abnormalities include hypercalciuria, hypocitraturia and hypomagnesuria. Urinary supersaturation indexes are often elevated and may prove to be a more precise predictor of stone recurrence than

traditional metabolic parameters.<sup>17,18</sup> Low urinary volume is also common and treatment should result in urine output of approximately 35 ml/kg daily.<sup>19</sup> Significant hypercalciuria and hypocitriuria should be aggressively treated in children with recurrent stone disease or signs of the presence of either multiple or bilateral calculi. Serum electrolyte evaluation is necessary in children found to have significant urine metabolic abnormalities.

Conservative management is most appropriate for stones of relatively small size (<4 mm) without signs of obstructive uropathy or urosepsis. It is important to have the child strain all urine so that calculus debris can be obtained and sent for stone analysis. This also gives an end point for conservative management possibly eliminating the need for follow-up radiographic assessment.

Once the child has been cleared of any calculus disease either through conservative management or surgical intervention, it is appropriate to obtain 2 consecutive 24-hour urine samples for metabolic stone risk profiling. These should include an internal creatinine standard to insure completeness of the urine sample. Traditional urinary metabolic parameters include calcium, phosphate, magnesium, citrate, creatinine, uric acid, pH, and voided volume. Pediatric reference ranges should be utilized when available. Serum evaluation should be performed in children with stone recurrence or multiple calculi, and should include calcium, phosphate, uric acid, creatinine, sodium, and potassium. Surgical intervention is appropriate with prolonged hangup of urinary stones or unrelenting symptoms such as pain, nausea, vomiting, and gross hematuria. Proactive treatment of renal stones >5 mm should be considered due to an increased risk of a stone this size causing obstructive symptoms while passing through the urinary system. Treatment strategies should be based upon accomplishing the best stone-free rate for the particular situation with the least morbidity and lowest risk for auxiliary procedures. The most effective treatment plan may include multiple modalities.

## **Treatment options**

### *ESWL*

Extracorporeal shock wave lithotripsy (ESWL) in children was first reported in 1988.<sup>20</sup> Initial reports in animal models indicated evidence of significant renal damage following SWL which may have contributed to the delay in its acceptance in children.<sup>21,22</sup> Long-term functional studies on pediatric patients following SWL show no significant change in effective renal plasma flow or mean body height at least 4 years after treatment.<sup>23–25</sup> The safety and efficacy of SWL has also been demonstrated in premature low-birth-weight infants.<sup>26</sup> Morphologic changes such as subcapsular or intrarenal hematomas have been infrequently noted, and usually resolve spontaneously within 1 week. It is not uncommon to experience gross hematuria after SWL, which quickly resolves with resumption of increased fluid intake. Any child with significant abdominal or flank discomfort in the early postoperative period should be evaluated for possible hematoma or obstruction from calculus debris.

Hemoptysis has also been reported postoperatively, particularly in children with significant orthopedic deformities.<sup>27</sup> Small stature and some skeletal deformities increase

the risk of the pulmonary field being present within the shockwave path. Prevention of such a complication may be lessened through the use of styrofoam padding, and some symptoms should resolve with conservative management.

Shockwaves are generated and focused by a variety of mechanical systems. The original units are spark gap generated, ellipsoid focused systems which are extremely powerful and have a wide focal point (Figure 64.4). This produces a wider area of shockwave effect, which increases the risk of complications. Subsequent generations of lithotriptors have improved both the scatter of energy and ease with which a child can be placed on the unit. Some units are portable and may be easily transported between operating room suites. In adults it is possible to perform shockwave lithotripsy under light anesthesia, although children may require a deeper general anesthetic for successful completion. Localization of the stone during treatment is determined by fluoroscopy, sonography, or plain x-ray films. Sometimes it is necessary to position a child prone in order to access the stone for effective lithotripsy.

Similar principles are applied to children as in adults, and proper patient selection will help to improve treatment outcomes. Some relative contraindications for SWL include morbid obesity, a large stone burden, increased



**Figure 64.4**

The original spark gap generated lithotripsy unit was quite effective but cumbersome. Refinements in technology have produced sleeker units capable of being transported between operating room suites.

stone density, congenital skeletal/renal anomalies, and previously failed SWL. The number of shocks, and the maximum energy level should be tailored for each case, and periodic stone visualization during the procedure will demonstrate when adequate lithotripsy has occurred. The primary goal always is to use the least amount of energy necessary to accomplish successful treatment.

### *Ureteroscopy*

Advances in the design of mini rigid and flexible ureteroscopes have resulted in miniaturization, allowing for use in pediatric patients. Digital imaging as well as enhancements to video technology now allow for clear visualization as well as instantaneous documentation of endourologic procedures (Figure 64.5). The first reported ureteroscopic procedure in an infant was in 1929 by Hugh Hampton Young.<sup>28</sup> He had performed the procedure in a 2-month-old boy with massively dilated ureters secondary to posterior urethral valves. He utilized a 9.5 F pediatric cystoscope and was able to visualize the ureter as well as intrarenal collecting system. It wasn't until 1988 that Ritchey and Shepherd independently published articles on the technique of pediatric ureteroscopy for treatment of urinary calculi.<sup>29,30</sup> Since this time, ureteroscopy has gained wide spread acceptance by pediatric urologists.

There exist two distinct types of ureteroscopes: mini rigid fiberoptic and flexible fiberoptic. The mini rigid fiberoptic (i.e. semirigid) ureteroscope has a metal outer casing, which is malleable enough to allow for limited bending without image distortion (Figure 64.6). These endoscopes are particularly useful in the distal ureter, but



**Figure 64.5** Modern day surgical rooms can be equipped with state of the art digital video equipment providing improved visualization as well as immediate documentation of endourologic procedures.

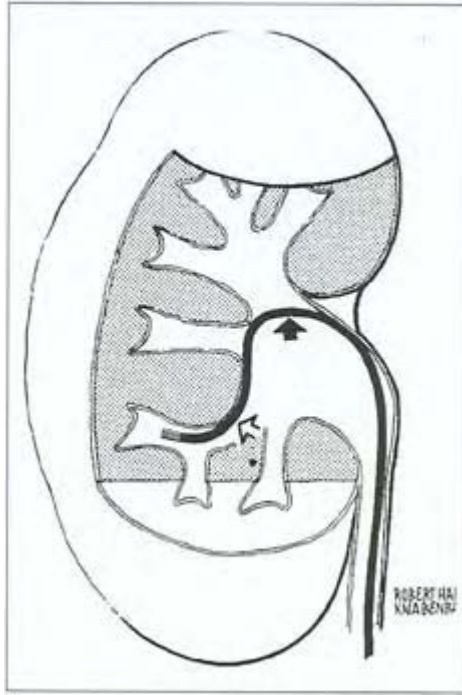


**Figure 64.6**

Semirigid ureteroscopes have an outside metal casing making them more resistant to damage when compared to flexible endoscopes. Fiberoptic image transmission and light delivery provides more room for irrigation and working channels. Many semirigid ureteroscopes can be autoclaved for sterilization.

may be difficult to pass into the proximal collecting system above the bony pelvis. Two working channels allow for simultaneous irrigation as well as placement of working instruments. Varying lengths are necessary, and this author uses both a 15 and 33 cm endoscope tailored to the child's size and location of the stone. These endoscopes are more durable than flexible ureteroscopes and most can be safely autoclaved for sterilization. The distal tip is as small as 4.7 F but the malleable metal shaft gradually increases in diameter as you move more proximally towards the eyepiece. Because of this it is necessary to maintain constant vigilance to help limit the risk of meatal injury in the young male infant.

Flexible ureteroscopes are useful within the proximal and intrarenal collecting system due to their active as well as passive tip deflection (Figure 64.7). Some models have the capability of both primary and secondary active deflec-



**Figure 64.7**

The open arrow demonstrates distal active deflection while the closed arrow shows passive secondary deflection enabling access into the lower pole calyx. Some models now have the capability of both primary and active secondary deflection.

tion, (our-8 Elite, circon, ACMI) and others have 270° primary deflection in either direction (Flex-ex, Karl Storz). Most flexible ureteroscopes have a working channel of approximately 3.6 F, which is adequate for passage of instruments while maintaining space for irrigation. Rarely is secondary passive tip deflection necessary for complete inspection of the intrarenal pediatric collecting system because the arc of deflection is adequate to access the lower pole in most pediatric kidneys (Figure 64.8). Many working instruments will decrease the ability to actively deflect the ureteroscope. It is important to remember to straighten the distal tip of the ureteroscope prior to passage of any working



instrument to help prevent damage. Resistance within the working channel may be decreased through the use of a silicone lubricant.

Because of their flexible design, these endoscopes are more prone to damage and need to be handled with care. Recent technologic advancements have improved the durability of both the outside sheath, and deflecting mechanisms, but have resulted in an increased outer diameter.



**Figure 64.8**

Most of the time only active deflection is necessary to access the lower pole calyx in the pediatric kidney.

Replacement of the fiberoptic bundles is necessary when the image becomes distorted, and any perforation of the working channel will cause damage to the endoscopes. Flexible endoscopes can be safely soaked in cold sterilization solution or undergo gas sterilization, but cannot be autoclaved. The distal tip is approximately 7.4 F but gradually becomes 8.5 F or greater at the proximal shaft, which helps to strengthen the sheath and protect the inner bundle fibers. This author prefers the use of three distinct lengths in children (35, 50, and 65 cm) in order to decrease the amount of redundant shaft outside of the body, which helps to prevent damage during use (Figure 64.9).

### **Working instruments**

A variety of working instruments have been designed for use within miniaturized endoscopes. Guidewires are the most commonly used working instruments in endourology. Not only do they aid in access to the ureter but they also help to prevent intraoperative complications by preventing loss of access to the collecting system. Most have an inner stainless steel core coated by polytetrafluoroethylene (PTFE) to reduce friction. Some have a super-elastic nitinol (nickle-titanium) alloy core which prevents

kinking of the wire. There are varying diameters, but a 150 cm 0.035 inch PTFE-coated guidewire with a 3 cm floppy distal tip is the most common type used in the author's practice. The distal tip may be straight or angled and the length of its flexible floppy tip varies. A dual floppy tip wire is the safest choice for passage of a flexible ureteroscope because it minimizes potential damage to the working channel.

A hydrophilic-coated guidewire is helpful for negotiating a tortuous or narrowed ureter and for placement of a working wire proximal to an impacted ureteral calculus. These extremely slippery guidewires need to be kept moist and should not be used as safety wires due to the ease with which they may be dislodged during an endoscopic procedure. Handling of the slippery hydrophilic wires is made easier through the use of a moistened gauze sponge. Extra-stiff guidewires are useful for straightening tortuous or reimplanted ureters (Figure 64.10) and also should be used for percutaneous tract dilatation. These wires should not be used when placing a flexible ureteroscope due to the increased risk of damaging the delicate working channel.

A variety of baskets as well as graspers have been developed to aid in extracting stone debris from the collecting system. They vary in diameter from 1.9–4.5 F and most are contained within a hydrophilic sheath (PTFE, Polyimide) to facilitate passage. A variety of designs of baskets exist, but the most significant improvement in basket design has been the tipless nitinol basket. The tipless design makes it particularly safe and useful for extraction of stones within a tight calyx and when deployed allows for near complete active deflection of the ureteroscope due its increased flexibility (Figure 64.11 A, B)<sup>31</sup>. Some of the newer baskets have been designed to allow controlled active angulation of the baskets' wires (Dimension, Bard Urological, Covington, GA) and others enable a canopy to form which may



**Figure 64.9**

Varying lengths of flexible endoscopes (35, 50, and 65 cm) are useful in pediatric ureteroscopy to help prevent damage to the endoscope by minimizing the amount of redundant flexible shaft present outside of the body.



**Figure 64.10**

An extra stiff guidewire helped to straighten this right reimplanted cross-trigonal ureter allowing for easier access during flexible ureteroscopy. Initial access to the reimplanted ureter can usually be obtained with the help of an angled tip guidewire.

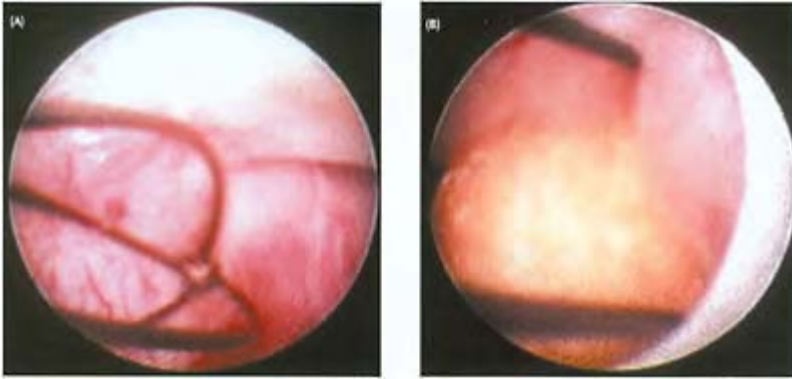
engage multiple small calculi. Some baskets have a central channel which allows for the simultaneous placement of electrohydraulic or laser lithotripsy probes once the stone is stabilized.

Grasping forceps are quite helpful during endoscopic stone extraction particularly within the ureter. The most significant advantage is that a grasper will disengage from a stone if it becomes lodged within a relatively narrow ureteral segment. This helps to prevent trauma of the ureteral wall by eliminating entrapment during stone removal. The grasper should be opened only as wide as is needed to engage the stone thus decreasing the risk of ureteral wall perforation (Figure 64.12). It is important to maintain contact with the stone while closing the graspers, therefore slight advancement of the sheath is needed as the forceps are closed.

Proper selection of a stone retrieval device is important for the successful and timely completion of any endoscopic procedure. Several factors impact this decision, particularly the size, position within the collecting system and condition (i.e. impacted vs nonimpacted) of the stone. Ptashnyk et al studied ex vivo porcine kidneys and ureters to determine which stone retrieval devices were most effective in certain situations.<sup>32</sup> Their conclusions were that graspers are most efficient at the removal of a single ureteral stone (particularly impacted) with little mucosal damage, and that a helical basket was most effective for Steinstrasse. In another study, nitinol baskets have been shown to be most effective for calyceal stones and those in the lower pole.<sup>33</sup> The flexible mitinol

component and the atraumatic tipless basket design allow complete deflection and produce minimal surrounding tissue trauma.

A newer instrument is the Dretler stone cone (Microvasive, Boston Scientific), which is a 0.038 inch



**Figure 64.11**

The strong, flexible, nitinol basket is easily deployed into a tight calyx (A) and produces minimal trauma to the urothelium when used to remove calculi (B). Nitinol baskets also enable near-complete active deflection of all flexible ureteroscopes.



**Figure 64.12**

A three-prong grasper is most effective at removing ureteral calculi. It is important to open the grasper only as wide as needed to engage the stone to

decrease the risk of ureteral wall perforation. The main safety feature of the grasper is that it will automatically become disengaged from the calculus if the stone becomes entrapped within a narrowed portion of the ureter.

Nitinol-teflon coated wire which can be coiled proximal to the calculus acting as a backstop to prevent proximal migration. It has been shown to be effective at extracting stone fragments and more successful than flat-wire baskets at preventing stone migration.<sup>34</sup>

Historically there are four modes of intracorporeal lithotripsy: ultrasonic; ballistic (i.e. pneumatic); electrohydraulic (EHL), and laser. Each has been extensively studied and all have unique capabilities and limitations.

Ultrasonic lithotripsy was first described in 1953.<sup>35</sup> The metal probe transmits vibrational energy to the tip, which when in contact with the stone results in disintegration due to cleavage of the crystal matrix. Small solid probes can be utilized through pediatric cystourethrosopes and large probes with a central suction channel are helpful for removal of stones during percutaneous procedures (Figure 64.13). These probes will lose energy transmission with any degree of bending, therefore are most effective when used in endoscopes with a straight working channel. Ultrasonic lithotripsy is safe and results in minimal tissue damage.<sup>36</sup> It is best suited for the percutaneous treatment of large renal stones.

Ballistic lithotripsy involves the pneumatic mechanical impaction of stones by a solid probe. There are no thermal or cavitation effects, therefore risk of tissue injury is minimal. This modality has been effective in fragmenting all types of stones and smaller flexible probes are



**Figure 64.13**

Ultrasonic lithotripsy probes can have a central channel which is helpful for the removal of stone debris during

treatment of calculi. Ultrasonic probes need to be used in an endoscope with a straight working channel to prevent the loss of energy due to bending of the device.

available.<sup>37-40</sup> Retrograde migration due to pneumatic impaction as well as loss of lithotripsy power with significant deflection of the probe are two significant shortcomings.

Electrohydraulic (EHL) lithotripsy was discovered by Yutkin in 1955 and involves the generation of an electrical spark, which produces a cavitation bubble, providing sufficient energy to produce lithotripsy<sup>41</sup> (Figure 64.14). The energy is maximized at a distance of approximately 1 mm from the stone and therefore the tip of the probe should be kept just off the surface of the stone. Electrohydraulic lithotripsy may not fragment all stone compositions but is



**Figure 64.14**

The generation of an electrical spark producing sufficient energy for lithotripsy is known as the process of electrohydraulic lithotripsy. The risk of tissue damage due to lateral disbursement of this energy is increased when working within the small confines of the pediatric collecting system.

able to be used through both flexible and rigid endoscopes. One significant risk of EHL is lateral disbursement of the energy, which can increase injury to the surrounding soft tissues. Probes are as small as 1.9 F which will allow access to lower pole calculi.

Holmium yttrium-aluminum-gar net (HO: YAG) laser lithotripsy is extremely effective at fragmenting all types of urinary calculi.<sup>42</sup> Holmium laser lithotripsy was first

reported in 1992<sup>43</sup> and subsequent reports have shown it to be safe in adults and children.<sup>44,45</sup> Holmium lithotripsy involves direct stone absorption of laser energy with subsequent disintegration.<sup>46</sup> Solid quartz fibers as small as 200  $\mu\text{m}$  enable near complete deflection of a flexible ureteroscope allowing access to nearly all parts of the collecting system. Larger fibers are helpful in the disintegration of larger stones contained within the kidney or bladder. Direct visualization of the tip of the probe is necessary to prevent subsequent endoscope or tissue damage during use. The fiber needs to be placed near the stone in order to result in fragmentation. Holmium laser lithotripsy results in dust particles and fragments less than 2 mm which should be able to pass spontaneously (Figure 64.15 A, B).

### Ureteroscopy technique

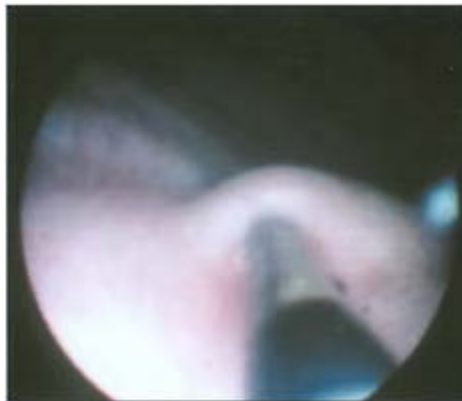
Ureteroscopy in children requires general anesthesia. After the child is placed in the dorsal lithotomy position, he or she is well padded in order to prevent excessive limb abduction or pressure on nerves. The male urethral meatus is carefully inspected and gently dilated if necessary. Cystoscopy is performed and the bladder is inspected and the position of ureteral orifices is visualized. A urine sample is obtained at the time of the cystoscopy and sent for urine culture.

The author first gauges the caliber of the ureteral orifice by using a 0.035 inch guidewire. If the orifice appears 'volcanic' and barely accepts a 0.035 guidewire, then either active dilatation or prestenosing of the ureter is performed (Figure 64.16). The ureter has three physiologic areas of narrowing with the narrowest portion being the orifice. These anatomic differences are age dependent and based on work by Cussen in 1971.<sup>47</sup> It is sometimes helpful to perform access to the ureteral orifice using two guidewires one inside the working channel and the other already independently placed in the ureter as a safety wire (Figure 64.17). This helps to control access and to increase the diameter by placing the endoscope directly between the two wires. Reports of balloon dilatation to 15 F has been previously reported with no significant complications or reflux, but clearly produces more active dilatation than actually necessary. This author prefers to use a graduated single-shaft dilator, which ranges from 6–10 F (Figure 64.18). Dilatation to 2 F sizes greater than the diameter of the endoscope is usually needed for successful access. Dilatation can be facilitated by performing this over a stiff guidewire or through a 13 F cystoscope sheath in order to prevent buckling within the bladder. If these maneuvers do not allow easy dilatation of the ureter, the author believes



**Figure 64.15**

Holmium laser energy is the most effective way to fragment stones. Dust fragments (A) will pass spontaneously. Larger stones can be precisely cleaved (B) into smaller sizes which facilitates intact removal.



**Figure 64.16**

It is often more prudent to present a ureter which only accepts a 3 F catheter





**Figure 64.17**

Dual wire access provides better expansion of the ureteral orifice enabling easier access to the proximal collecting system. One wire is placed through the working channel of the endoscope which helps to safely guide the semirigid ureteroscope.

it is more prudent to place a ureteral stent to passively dilate the ureter rather than performing significant active balloon dilatation. Dilatation of the ureter maybe required in approximately 30% of children undergoing ureteroscopy.<sup>48</sup>

When therapeutic maneuvers are anticipated it is important to maintain a safety guidewire within the ureter.



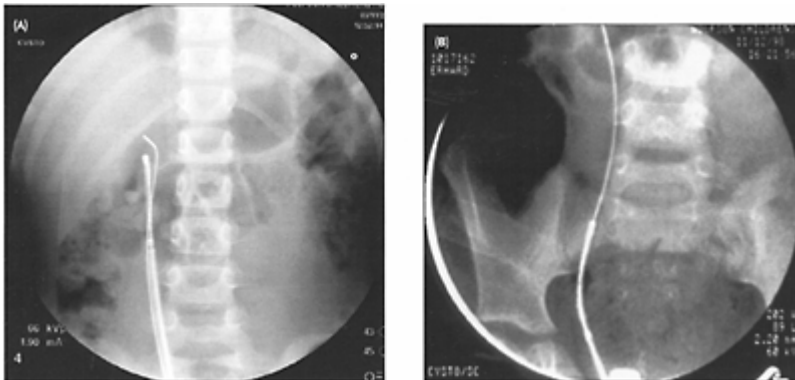
**Figure 64.18**

A 6–10 F soft graduated (above) and 10 F dual lumen catheter (below) are

## two helpful tools used for accessing the pediatric ureter.

A hydrophilic guidewire may aid in accessing a tortuous ureter or one with an impacted stone, but should not be used as a routine safety wire due to the ease with which it may become dislodged. A flexible ureteroscope requires either the use of an access sheath or a second working guidewire for placement of the ureteroscope into the proximal collecting system (Figure 64.19 A, B) The smallest sheath which accepts flexible ureteroscopes is 9.5 F, therefore, in children, prestenring of the ureter is often required in order to dilate the ureter to allow the safe use of an access sheath. Access sheaths should be used with caution and are most helpful when it will be necessary to traverse the ureteral orifice many times when treating large or multiple stones in the proximal collecting system. Fluoroscopic guidance is absolutely necessary during any ureteroscopic procedure.

Previous urologic surgery involving either the bladder neck, ureter, urethra, or ureteropelvic junction is not a contraindication for ureteroscopy. A child who has undergone previous hypospadias surgery may require urethral dilatation prior to placement of the ureteroscope if there is meatal stenosis. It is important to use small diameter endoscopes to avoid disruption of previous bladder neck reconstruction. Oftentimes children who have had bladder neck reconstruction have had ureteral reimplantation at the time of their primary surgery and care must be taken not to over-torque the bladder neck when accessing the previously reimplanted ureter. Access to the ureter after previous reimplantation is clearly dependent upon the type of surgery performed. When either an advancement or extravesical procedure was utilized, access is similar to the unoperated child. When a previous cross-trigonal reimplantation has been performed, access can be more difficult. In this instance, the ureteral orifice is usually laterally located and can be cannulated with an angled guidewire. If this is unsuccessful an actively deflecting guidewire can be utilized. Once access has been gained the



**Figure 64.19**

An access sheath is pictured here with a flexible endoscope exiting the

proximal portion of the sheath (A). The safety wire is placed outside of the sheath which provides the largest internal lumen for endoscope placement and stone removal. Access to the proximal collecting system is most often accomplished using a guidewire in a monorail fashion (B). One guidewire is used when a diagnostic procedure is being performed, but two guidewires are necessary when the therapeutic intervention is planned.

initial wire should be replaced with a stiff guidewire which then straightens the intramural portion of the ureter allowing access for ureteroscopy. Dilatation of the tunnel is usually not necessary although it is sometimes necessary to dilate the ureteral orifice. When the procedure is finished the ureter will return to its preoperative cross-trigonal position (Figure 64.20). Recurrent reflux after ureteroscopy in the previously reimplanted ureter has not been demonstrated.

Intrarenal access after previous ureteropelvic junction repair is usually straightforward as long as there has been adequate healing and success of the previous surgery. The ureter remains supple at the site of previous repair and is at no greater risk of injury. Postoperative stenting is not always required, but should be performed after procedures requiring either extensive manipulation or significant active dilatation. If a stent is left in place, the author prefers to leave a dangle string attached to facilitate removal without anesthesia in the office approximately 1 week after the procedure.

A mini rigid ureteroscope should be used for distal and midureteral calculi. It may be used for more proximal stones if it can be successfully passed above the pelvic brim. Flexible ureteroscopy is necessary most of the time for proximal ureteral calculi and should always be used for stones contained within the intrarenal collecting system. Complete access to the intrarenal system is usually accomplished through active deflection alone. Rarely is



**Figure 64.20** The cross-trigonal appearance of the right reimplanted ureter is maintained after flexible ureteroscopy. Postoperative reflux has not been an issue in those children who have undergone ureteroscopy after previous ureteral reimplantation.

secondary passive deflection necessary in the smaller pediatric kidney. Instillation of contrast during ureteroscopy will guide you during the complete inspection of the collecting system under fluoroscopy.

Once the stone is encountered it is important to gauge the size of the stone versus the diameter of the ureter. Many ureteral stones can be removed intact through basket or grasper manipulation provided the caliber of the distal ureter is adequate to allow atraumatic retrieval. For stones, which are either impacted or are too large to remove intact, in situ Holmium laser lithotripsy is performed. For an impacted stone, attempts should be made to dislodge the stone into the proximally dilated portion of the ureter. This will allow more room for laser lithotripsy, and decrease the risk of complications. Once the stone is dislodged, the jagged surface is either precisely treated to smooth out rough edges or the entire stone can be cleaved into distinct fragments for subsequent removal. Stones that cannot be dislodged should be treated first on its periphery which should disimpact the stone. It is important to retrieve at least one stone fragment for crystallographic analysis, and once this is achieved it is more efficient to deposit subsequent small fragments within the bladder, which should pass spontaneously. If a stone fragment becomes displaced outside the ureteral wall due to perforation, it is prudent to abandon further attempts at extraction of the migrated calculus.

*Percutaneous endourology*

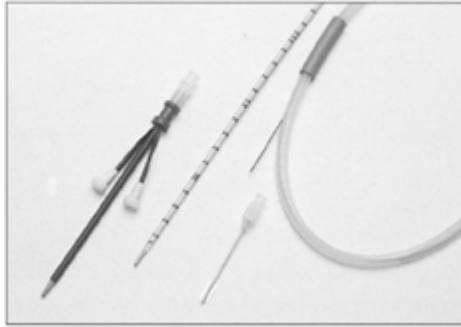
Thomas Hillier in 1865 is credited with the description of the first therapeutic percutaneous renal drainage of what was described as ureteropelvic junction obstruction.<sup>49</sup> Unfortunately, after 4 years of periodic percutaneous drainage the young boy succumbed to septicemia at age 8. It wasn't until 1941 that Rupel described the removal of renal calculus debris through a nephrostomy tract using endoscopic equipment.<sup>50</sup> Percutaneous drainage of hydronephrosis was again reported by Goodwin in 1955, and it wasn't until 1985 that Woodside et al. presented a series of 7 pediatric patients who had undergone a percutaneous procedure.<sup>51</sup>

Early on, percutaneous stone removal was limited to children 8 years of age and older due to fears of significant blood loss and increased renal damage with large (>24 F) tract dilatation.<sup>52</sup> The defect created by a 24 F tract in a child's kidney corresponds to a 72 F defect in an adult kidney.<sup>53</sup> Increased tract size is directly correlated with increased complication rates, although no significant renal scarring or functional changes can be readily detected after large tract dilatation.<sup>54,55</sup> Subsequent reports have demonstrated that percutaneous procedures are technically feasible for children less than 8 years of age, and that complications can be decreased by utilizing a tract <22 F.

Because of concerns regarding hematologic complications, the technique of a smaller access percutaneous procedure has been developed. Helal et al. presented their experience using a 15 F peel away sheath in a 2-year-old child for percutaneous stone removal.<sup>56</sup> A smaller 11 F technique using a 'mini perc' approach has also been reported (Figure 64.21). Access to the collecting system is thought to be less traumatic because of the smaller caliber site. There have been no reports of bleeding complications in uncomplicated procedures after mini perc intervention, and the need for postoperative percutaneous nephrostomy drainage is often eliminated. Treatment of large (>3 cm) stones can be tedious, therefore a larger peel-away sheath (15–22 F) is recommended to expedite stone fragment removal.

Most pediatric percutaneous procedures are performed for management of renal calculi. It is important that these procedures be performed in an institution where there is an endourologist and interventional radiologist experienced in the treatment of children. Needle access to the kidney is required for tract dilatation and therapeutic intervention, and there is some suggestion that obtaining early access (one day prior to surgery) may decrease bleeding as well as operative time. This is particularly helpful for a 'mini-perc' procedure because the smaller field of view becomes easily obscured by minimal bleeding. Nevertheless, it is possible to obtain access at the time of percutaneous intervention, which does result in safe completion of the procedure.

The proper site chosen for percutaneous access should allow both a direct route to the stone and permit easy access to other areas of the collecting system. The optimal position is usually a posterior calyx with a wide, straight infundibulum. Multiple sites may be necessary, and should be utilized when there is a complete staghorn calculus or any intrarenal anomalies making it difficult to access all stone containing calyces through a single site. Hematologic complications requiring transfusion are not increased when multiple sites are utilized.<sup>57</sup> It is important to obtain the primary access site where it will be possible to maxi-



**Figure 64.21**

This prepackaged mini percutaneous access set is available from Cook Urological, Spencer, Indiana.

mally debulk the stone burden, and secondary sites where calyces will be difficult to reach through the primary tract. If the stones are contained within a calyceal diverticulum or a calyx with a narrowed infundibulum, it is necessary to have direct access into that part of the collecting system. Upper pole access sites should be used with caution because of the increased risk of pneumo/hydrothorax. Because of this, a chest x-ray should be obtained at the conclusion of any percutaneous procedure involving upper pole access.

Once needle access has been obtained, a wire is passed down the ureter into the bladder to allow a controlled tract dilatation and to avoid the accidental loss of access to the collecting system. Slippery hydrophilic guidewires should be exchanged for standard teflon coated wires prior to dilatation. The use of a stiff guidewire will facilitate dilatation. If ureteral access is not possible or if access is obtained into an obstructed system or calyceal diverticulum, multiple coils of the wire should be placed within the contained collecting system prior to tract dilatation.

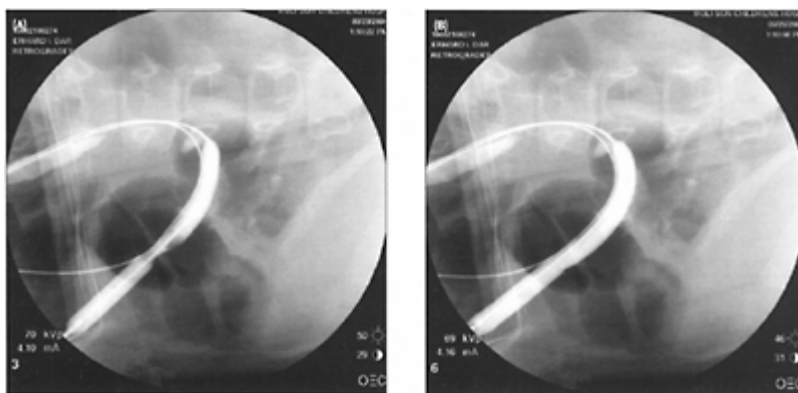
Once safe access has been confirmed, the tract is dilated either using sequential graduated dilators (Amplatz), or active balloon dilatation. Both techniques have proven safe and efficacious, but sequential dilatation of larger tracts may be at increased risk for bleeding due to the potential sheering effect of this technique. Constant vigilance under fluoroscopy is necessary to make certain that dilatation is not carried too far medially, therefore, avoiding disruption of the renal pelvis. The small nondilated pediatric kidney is at greatest risk for this complication and extreme caution must be undertaken to help prevent such occurrences. If there is significant disruption of the renal pelvis or UPJ, it may be necessary to abandon the procedure and to place a temporary nephrostomy or nephroureteral stent.

For balloon dilatation, the distal radiographic marker is placed into the renal pelvis while the proximal portion of the balloon is located externally. The balloon is then inflated to its maximum pressure and then left fully inflated until there is no longer any evidence of fascial constriction (Figure.64.22 A, B). The balloon is kept inflated for several minutes to help aid in hemostasis. The access sheath can be placed into the pelvis

over the balloon once it has been partially deflated. The balloon size should correlate with the size of the sheath to be used.

If there is any significant bleeding encountered after dilatation, it may be necessary to temporarily place either a large Foley catheter or a tamponade balloon. If these techniques do not result in satisfactory hemostasis, it will be necessary to leave the catheter in place and perform the therapeutic intervention at another time. Uncontrolled hemorrhage requiring transfusion should be evaluated with angiography for possible vascular embolization.

After the working sheath has been placed, the planned procedure is then undertaken. Both rigid as well as flexible instrumentation may be necessary and should be present in the operating room suite in case the need arises. If there is a



**Figure 64.22**

Percutaneous access is facilitated through the use of balloon dilators. Once you have confirmed proper positioning under fluoroscopy, dilute contrast is used to expand the balloon and is monitored under fluoroscopy. Initial fascial constriction (A) is noted, and the balloon is continued to be inflated to its maximum pressure until all constriction has been eliminated (B). The size of the balloon should be slightly larger than the size of the sheath to be utilized.

large stone burden, then the procedure will be facilitated through placement of a 22 F sheath. This allows access with an adult nephroscope enabling the use of larger

instrumentation, and giving the capability of removing large intact stone fragments (Figure 64.23). If a 'mini-perc' procedure is performed through an 11 F peel-away sheath, then either an offset pediatric cystoscope with a straight working channel or 9.5 F modified mini rigid ureteroscope will be necessary to access the kidney. The straight channel offset lens endoscope will allow for the passage of ultrasonic and ballistic lithotripsy probes whereas the in-line mini rigid cystoureteroscope will require the use of the Holmium laser, electrohydraulic, or flexible ballistic lithotripsy devices for stone fragmentation. This author prefers the inline endoscope because it has two working channels, which allows simultaneous suction irrigation (5.4 F), and lithotripsy (2.3 F). It also permits 360° rotation of the endoscope for maximum positioning of lithotripsy probes. The endoscope used should be several French sizes less than the internal diameter of the sheath in order to allow continuous flow around the scope, which lessens the risk of significant extravasation. The use of the warmed saline irrigant is encouraged, and this will need to be changed to water or glycine if an electrosurgical procedure is planned. Electrohydraulic lithotripsy is equally effective in saline or water, and thus saline should be used to avoid hyponatremia. Levering of the nephroscope should be limited in order to avoid injury to the infundibulum as well as renal parenchyma during the percutaneous procedure.

Endourologic instrumentation is similar to that used for other procedures. The Holmium laser is particularly useful during small caliber percutaneous access procedures in order to debulk large stone burdens. Extraction of stone fragments is facilitated by using a 4.5 F nitinol basket. Ultrasonic lithotripsy is quite safe and can be performed



**Figure 64.23**

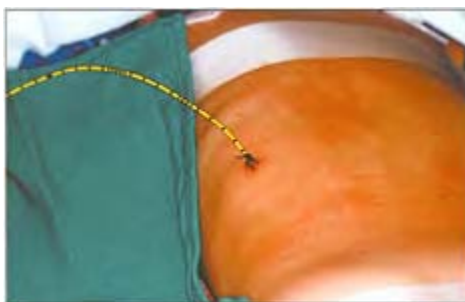
Fiberoptic offset nephroscopes provide access utilizing a 22 F sheath while performing percutaneous stone removal. Fiberoptic technology has resulted in the decreased diameter of the outer sheath while maintaining a large central channel for completion of the procedure.



through the straight working channel of either a small-caliber offset cystourethroscope or an adult percutaneous nephroscope. Attempts should be made to remove all stone fragments greater than 2 mm in order to limit a potential nidus for stone regrowth or obstruction with passage of a large fragment. Complete visualization of the intrarenal collecting system as well as ureter should be undertaken. This usually requires the use of a flexible endoscope. Complete inspection is sometimes hampered by limitations of the size of the pediatric kidney and size of the percutaneous access sheath. Significant clots may obscure stone fragments, therefore, every attempt should be made to irrigate them free to allow complete visualization. Most of the time it is necessary to leave a percutaneous nephrostomy tube in place at the completion of the procedure, but it is possible to limit its use. (Figure 64.24) Access to the kidney should be maintained until postoperative x-rays confirm that no second look procedure will be needed.

### Treatment strategies

Many factors need to be considered when deciding the proper treatment modalities for urinary tract calculi in children. Not only do you have to consider the characteristics of the stone (size, shape, location, density, number, etc.), but you also have to look at the characteristics of the child. Body habitus, as well as associated congenital and acquired conditions need to be taken into consideration. Surgeon expertise and available technology may also guide treatment strategy. Each case needs to be individualized in order to choose the best form of treatment in regards to shockwave lithotripsy vs retrograde ureteroscopy vs. an antegrade percutaneous approach.



**Figure 64.24**

Placement of a nephrostomy tube is not always necessary after small access percutaneous procedures, but it is important to maintain access to the kidney and ureter until postoperative x-rays confirm that no secondary percutaneous procedure is necessary.

*Renal calculi*

Shockwave lithotripsy is the least invasive form of therapy which offers reasonable stone-free rates of greater than 80% with minimal complications.<sup>58-64</sup>

Stones <1 cm are most efficaciously treated by this modality and often require a single treatment. Higher retreatment rates and the need for ancillary procedures is seen with large stone burdens and in children with renal or collecting system abnormalities.<sup>64,65</sup> Therefore, SWL is not the best therapy when there is evidence of UPJ obstruction, calyceal diverticulum, or infundibular stenosis. SWL is also less effective for ectopic and horseshoe kidneys because of difficulties with precise energy delivery (increased surrounding bony and soft tissue structures) and the presence of an abnormally rotated collecting system which may prevent post-treatment stone clearance. In addition, alternative therapies to SWL should be considered for extremely dense stones (brushite, cystine)<sup>66</sup> and those calculi within an abnormal lower pole (i.e. long, narrowed infundibulum). In these instances the energy may not be sufficient for adequate lithotripsy, and the abnormal intrarenal anatomy may promote fragment retention. Currently, it appears that SWL is best suited for solitary renal stones  $\leq 1.5$  cm not contained within an abnormal lower pole calyx, and not associated with any congenital or acquired renal abnormalities. Despite this, SWL monotherapy for the treatment of staghorn calculi has been shown to be effective, with stone-free rates of approximately 88% after multiple treatment sessions.

The role of ureteroscopy for the treatment of renal calculi in children remains to be defined. Several reports have demonstrated ureteroscopy to be an effective treatment for stones throughout the entire intrarenal collecting system. It has been successful for the treatment of stone-containing calyceal diverticula of the mid and upper pole.<sup>67</sup> Primary ureteropyeloscopy with stone removal should also be performed when ureteroscopy is being used to treat other ureteral stones. This enables easy access to the kidney for treatment and provides the greatest chance of success with one procedure. Residual fragments after SWL, or failure of SWL as the primary procedure are two other reasons to perform ureteropyeloscopy for stone removal. As mentioned previously, placement of a ureteral access sheath in a presented ureter may facilitate removal of large stones. Concomitant UPJ or intrarenal obstruction can also be treated endoscopically at the time of stone removal.

For intrarenal stones >1 cm, multiple large calculi, staghorn calculi, children with urinary tract malformations or previous reconstruction, a percutaneous approach may be better suited. Stone-free rates after a single percutaneous session range anywhere from 70–100%.<sup>54,68-72</sup> For large stones and staghorn calculi, combined 'sandwich' therapy (percutaneous stone removal followed by shockwave lithotripsy), provides stone-free rates greater than 90%. A percutaneous procedure does carry risks of excessive bleeding requiring transfusion, but several series have shown that utilization of a tract less than 22 F significantly limits this risk. Multiple percutaneous sites may be necessary for complete access to the stone, and have been shown not to increase the risk of transfusion. Long term follow up supports percutaneous procedures as being safe with no significant damage to the pediatric kidney.

Laparoscopy in children has become more widespread and has recently been reported in the management of renal calculi.<sup>73</sup> Patient selection criteria included stones greater than 2.5 cm with failure of percutaneous renal access. Not only does laparoscopy provide

a high stone free rate, but also enables the repair of concomitant ureteropelvic junction obstruction. Laparoscopy may also prove helpful in the management of large peripheral calyceal diverticula containing stones by allowing surgical unroofing with ablation of the diverticular neck and lining. Further experience should better define the role of laparoscopy in the treatment of pediatric stone disease.

### *Ureteral calculi*

Experience with shockwave lithotripsy for stones contained within the ureter has been shown to be effective 54–100% of the time. Retreatment rate for stones within the ureter is necessary up to 23% of the time. Patient positioning may need to be modified for distal ureteral stones by placing the child in the prone position. Stones over the bony pelvis are difficult to treat using SWL because of inadequate visualization and lack of adequate energy delivery.

A review of the literature shows that the stone free rate after pediatric ureteroscopic lithotripsy is 77–100%.<sup>45,48,74–85</sup> Advances in both endoscopic instrumentation as well as Holmium laser lithotripsy have been the major reasons why there has been increased success. One appealing aspect of the ureteroscopic removal of stones is that it offers an immediate stone-free condition at the completion of the procedure. The American Urological Association has issued guidelines to standardize the management of adult patients with stones and Vansavage et al.<sup>82</sup> have published their recommendations for the modification of these guidelines when applying it to the pediatric patient. The ureteroscopic removal of stones contained within the ureter is clearly safe and effective and should be considered the first line treatment for most children.

The percutaneous removal of ureteral stones is rarely indicated. It should be considered the primary form of therapy for children who have impacted stones with significant hydroureteronephrosis and urinary tract infection or urosepsis. The antegrade approach allows for prompt decompression of the obstructed collecting system with antegrade ureteroscopic access for subsequent removal. The technique for antegrade ureteroscopy is exactly the same for the retrograde approach, and has been discussed previously. Flexible rather than minirigid endoscopy should be utilized for antegrade ureteroscopy to limit potential complications.

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Abbreviations: ADPKD=autosomal dominant polycystic kidney disease; BPH=benign prostatic hyperplasia; CT=computed tomography; ESWL=extracorporeal shock wave lithotripsy; HIFU=high-intensity focused ultrasound; MRI=magnetic resonance imaging; PSA= prostate-specific antigen; TURP=transurethral resection of prostate; UPJ=ureteropelvic junction; UTI=urinary tract infection

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